FORM PTO-1390 (REV 5-93) — U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	
U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5)	09/242843

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/GB97/02284	27 August 1997 (27.08.97)	29 August 1996 (29.08.96)

TITLE OF INVENTION
PESTICIDAL AGENTS

APPLICANT(S) FOR DO/EO/US
JARRETT, Paul; ELLIS, Deborah June; MORGAN, James Alun Wynne

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [X] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [X] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US)
6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [ ] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [ ] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [X] Other items or information:
    - Amendments to the claims of the International Application under PCT Article 34(2)(b) are transmitted herewith

80 Rec'd PCT/PTO 25 FEB 1999

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/242843	PCT/GB97/02284	

17. ☒ The following fees are submitted:

Basic National Fee (37 CFR 1.492(a)(1)-(5)):

Search Report has been prepared by the EPO or JPO **$830.00**

International preliminary examination fee paid to USPTO (37 CFR 1.482) **$640.00**

No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)).. **$710.00**

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37CFR 1.445(a)(2)) paid to USPTO......... **$950.00**

International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2)-(4)............ **$90.00**

				CALCULATIONS		PTO USE ONLY
ENTER APPROPRIATE BASIC FEE AMOUNT =				$ 840	00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☒ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				$ 130	00	
Claims	Number Filed	Number Extra	Rate			
Total Claims	36 -20 =	16	X $18	$ 288	00	
Independent Claims	7 -3 =	4	X $78	$ 234	00	
Multiple dependent claims(s) (if applicable)			+ $230.00	$		
TOTAL OF ABOVE CALCULATIONS =				$ 1492	00	
Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$	-	
SUBTOTAL =				$ 1492	00	
Processing fee of **$130.00** for furnishing the English translation later the ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$		
TOTAL NATIONAL FEE =				$ 1492	00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$		
TOTAL FEES ENCLOSED =				$ 1492	00	
				Amount to be: refunded	$	
				charged	$	

a. ☒ A check in the amount of $ 1492.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. ______________ in the amount of $______________ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 04-1406. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

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REGISTRATION NUMBER

09/242843
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	)	
	)	Examiner:
PAUL JARRETT et al.	)	Not Yet Assigned
	)	
Application No. Not Yet Assigned	)	
[International Appln. No. PCT/GB97/02284]	)	Group Art Unit:
	)	Not Yet Assigned
Filed: Concurrently Herewith	)	
[International Filing Date: 27 August 1997]	)	
	)	
For: PESTICIDAL AGENTS	)	

PRELIMINARY AMENDMENT

Before calculation of the filing fee, please amend the claims of the above-referenced patent application, which claims are based on the Article 34 claim amendments filed in the corresponding international patent application, as follows:

Claim 3, line 1, delete "or claim 2";

Claim 4, lines 1-2, delete "any one of the preceding claims" and insert - - claim 1 - -;

Claim 5, lines 1-2, delete "to any one of the preceding claims" and insert - - claim 1 - -;

Claim 6, line 1, delete "any one of claims 1 to 4" and insert - - claim 1 - -;

Claim 7, lines 1-2, delete "any one of the preceding claims" and insert - - claim 1 - -

Claim 11, lines 1-2, delete "any one of the preceding claims" and insert - - claim 1 - -;

Claim 12, delete "10" and insert - - 11 - -;

Claim 14, delete "12" and insert - - 13 - -;

Claim 20, line 2, delete "or claim 19";

Claim 21, line 2, delete "any one of claims 17 to 20" and insert - - claim 17 - -;

Claim 24, line 2, delete "any one of claims 21 to 23" and insert - - claim 21 - -;

Claim 27, line 3-4, delete "any one of claims 17 to 20" and insert - - claim 17 - -;

Claim 29, lines 2-3, delete "any one of claims 25 to 28" and insert - - claim 25 - -;

Claim 30, lines 2-3, delete "any one of claims 25 to 28" and insert - - claim 25 - -;

Claim 32, line 2, delete "any one of claims 17 to 20" and insert - - claim 17 - -;

Please add the following new claims:

33. A recombinant DNA which encodes a pesticidal agent according to claim 18.

34. A recombinant DNA of claim 33 which comprises the sequence of Figure 2 or a variant or fragment thereof.

35. A host organism comprising a nucleotide sequence coding for a fusion

protein comprising a pesticidally active portion of an agent as claimed in claim 18 in combination with other pesticidal proteinaceous toxicity enhancing materials.

36. A host organism as claimed in claim 35 wherein the pesticidal toxicity enhancing materials comprise delta-endotoxin from B. thuringiensis.

REMARKS

The purpose of this Preliminary Amendment is to delete multiple claim dependencies.

Dependent claims 33-36 have been added and relate to a recombinant DNA encoding a pesticidal agent according to claim 18 and a host organism having a nucleotide sequence coding for a fusion protein comprising a pesticidally active portion of such an agent. Support for these four additional claims can be found in original claims 21, 22, 27 and 28.

Favorable consideration leading to prompt allowance of the present application is respectfully requested.

Respectfully submitted,

DANN, DORFMAN, HERRELL AND SKILLMAN
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CLAIMS:

1. An insecticidal composition which:
(i) is adapted for oral administration to an insect,
(ii) comprises a proteinaceous pesticidal material obtainable from a *Xenorhabdus* species, or a pesticidal fragment thereof, or a pesticidal variant or derivative of either of these,
having in each case toxic activity when administered orally.

2. A composition according to claim 1 wherein the said pesticidal material comprises material encoded by the nucleotide sequence of Figure 2 or variant or fragment thereof, or a sequence which hybridises with said sequence.

3. A composition according to claim 1 or claim 2 which comprises cells of *Xenorhabdus*.

4. A composition as claimed in any one of the preceding claims which comprises supernatant taken from cultures of cells of *Xenorhabdus* species.

5. A composition according to any one of the preceding claims wherein the *Xenorhabdus* species is *Xenorhabdus nematophilus*.

6. A composition according to any one of claims 1 to 4 wherein the *Xenorhabdus* species is ATCC 19061, NCIMB 40886 or NCIMB 40887.

7. A composition as claimed in any one of the preceding claims which comprises a further pesticidal material not obtainable from *Xenorhabdus*.

8. A composition according to claim 7 wherein the said further pesticidal material comprises a material obtainable from *B. thuringiensis*.

AMENDED SHEET
IPEA/EP

28. A host organism as claimed in claim 27 wherein the pesticidal toxicity enhancing materials comprise delta-endotoxin from B. thuringiensis.

29. A host organism as claimed in any one of claims 25 to 28 wherein the host is a plant.

30. A host organism as claimed in any one of claims 25 to 28 wherein the host is a virus pathogenic to insects.

31. A fusion protein as expressed by a host as claimed in claim 27.

32. A pesticidal composition comprising one or more agents as claimed in any one of claims 17 to 20.

PESTICIDAL AGENTS

The present invention relates to materials, agents and compositions having pesticidal activity which derive from bacteria, and more particularly from *Xenorhabdus* species. The invention further relates to organisms and methods employing such compounds and compositions.

There is an ongoing requirement for materials, agents, compositions and organisms having pesticidal activity, for instance for use in crop protection or insect-mediated disease control. Novel materials are required to overcome the problem of resistence to existing pesticides. Ideally such materials are cheap to produce, stable, have a high toxicity (either when used alone or in combination) and are effective when taken orally by the pest target. Thus any invention which provided materials, agents, compositions or organisms in which any of these properties was enhanced would represent a step forward in the art.

Xenorhabdus spp. in nature are frequently symbiotically associated with a nematode host, and it is known that this association may be used to control pest activity. For instance, it is known that certain *Xenorhabdus spp.* alone are capable of killing an insect host when injected into the host's hemocoel.

In addition, one extracellular insecticidal toxin from *Photorhabdus luminescens* has been isolated (this species was recently removed from the genus *Xenorhabdus*, and is closely related to the species therein). This toxin is not effective when ingested, but is highly toxic when injected into certain insect larvae (see Parasites and Pathogens of Insects Vol.2, Eds. Beckage, N. E. et al., Academic Press 1993).

ARTICLE 34

Also known are certain low-molecular weight heterocyclic compounds from *P.luminescens* and *X.nematophilus* which have antibiotic properties when applied intravenously or topically (see Rhodes, S.H. et al., PCT WO 84/01775).

Unfortunately none of these prior art materials have the ideal pesticide characteristics discussed above, and in particular, they do not have toxic activity when administered orally.

The present invention provides pesticidal agents and compositions from *Xenorhabdus* species, organisms which produce such compounds and compositions, and methods which employ these agents, compositions and organisms, that alleviate some of the problems with the prior art.

According to one aspect of the present invention there is disclosed a method of killing or controlling insect pests comprising administering cells from *Xenorhabdus* species or pesticidal materials derived or obtainable therefrom, orally to the pests.

A PCT application of CSIRO published as WO 95/00647 discloses an apparently toxic protein from *Xenorhabdus nematophilus*; however no details of the protein's toxicity are given, and certainly there is no disclosure of its use as an oral insecticide.

Thus the invention provides an insecticidal composition which:

(i) is adapted for oral administration to an insect,
(ii) comprises a proteinaceous pesticidal material obtainable from a *Xenorhabdus* species, or a pesticidal fragment thereof, or a pesticidal variant or derivative of either of these,

having in each case toxic activity when administered orally.

The composition may in fact comprise cells of *Xenorhabdus* or alternatively supernatant taken from cultures of cells of *Xenorhabdus* species. However, the composition

preferably comprises toxins isolable from *Xenorhabdus* as illustrated hereinafter. Toxic activity has been associated with material encoded by the nucleotide sequence of Figure 2. Thus, the composition suitably comprises a pesticidal material which is encoded by all or part of the nucleotide sequence of Figure 2. Pesticidal fragments as well as variants or derivatives of such toxins may also be employed.

The sequence of Figure 2 is of the order of 40kb in length. It is believed that this sequence may encode more than one protein, each of which may regulate or be insecticidal either alone or when presented together. It is a matter of routine to determine which parts are necessary or sufficient for insecticidal activity.

As used herein the term ``variant'' refers to toxins which have modified amino acid sequence but which share similar activity. Certain amino acids may be replaced with different amino acids without altering the nature of the activity in a significant way. The replacement may be by way of ``conservative substitution'' where an amino acid is replaced with an amino acid of broadly similar properties, or there may be some non-conservative substitutions. In general however, the variants will be at least 60% homologous to the native toxin, suitably at least 70% homologous and more preferably at least 90% homologous.

The term ``derivative'' relates to toxins which have been modified for example by chemical or biological methods.

These toxins are novel, and they and the nucleic acids which encode them form a further aspect of the invention.

A preferred *Xenorhabdus* species is the bacteria *X.nematophilus*. Particular strains of *X.nematophilus* which are useful in the context of the invention are

ATTC 19061 strain, available from the National Collection of Industrial and Marine Bacteria, Aberdeen, Scotland (NCIMB). In addition, suitable strains include two novel strains of *Xenorhabdus* which were deposited at the NCIMB on 10 July 1997 and were designated with repository numbers NCIMB 40886 and NCIMB 40887. These latter strains form a further aspect of the invention.

All strains have common characteristics as set out in the following Table 1.

Table 1

	Strains		
Characteristics	ATCC 19061	NCIMB 40887	NCIMB 40886
Gram strain	negative	negative	negative
Shape/size	rods up to 4µm long	rods up to 4µm long	rods up to 4µm long
Motile	Yes	Yes	Yes
Bioluminescent	No	No	No
Colour on NBTA*	blue	blue	blue
insecticidal on ingestion by insects	yes	yes	yes
Production of Antibiotics	yes	yes	yes
Resistant to ampicillin (50µg/ml)	yes	yes	yes
colony morphology/ colour	circular convex cream	circular convex cream	circular convex cream

*NBTA (Oxoid nutrient agar containing 0.0025% bromothymol blue and 0.004% tetrazolium chloride)

Preferably the pest target is an insect, and more preferably it is of the order Lepidoptera, particularly

Pieris brassicae, *Pieris rapae*, or *Plutella xylostella* or the order *Diptera*, particularly *Culex quinquefaciatus*.

In a preferred embodiment of the invention, cells from *Xenorhabdus* species or agents derived therefrom are used in conjunction with *Bacillus thuringiensis* as an oral pesticide.

In further embodiments, rather than using *Bacillus thuringiensis* itself, pesticidal materials obtainable from *B.thuringiensis* (e.g. delta endotoxins or other isolates) are used in conjunction with *Xenorhabdus* species.

The term 'obtainable from' is intended to embrace not only materials which have been isolated directly from the bacterium in question, but also those which have been subsequently cloned into and produced by other organisms.

Thus the unexpected discovery that bacteria of the genus *Xenorhabdus*(and materials derived therefrom) have pesticidal activity when ingested, and that such bacteria and materials can be used advantageously in conjunction with *B.thuringiensis* (and toxins or materials derived therefrom), forms the basis of a further aspect of the present invention. The pesticidal activity of *B.thuringiensis* isolates alone have been well documented. However, synergistic pesticidal activity between such isolates and bacteria of the *Xenorhabdus* species (or materials derived therefrom) has not previously been demonstrated.

In still further embodiments of the invention, culture supernatant taken from cultures of *Xenorhabdus* species, particularly *X. nematophilus*, is used in place of cells from *Xenorhabdus* species in the methods above.

All of these methods can be employed, inter alia, in pest control.

The invention also makes available pesticidal compositions comprising cells from *Xenorhabdus* species, preferably *X.nematophilus*, in combination with *B. thuringiensis*. As with the methods above, a pesticidal toxin from *B.thuringiensis* (preferably a delta endotoxin) may be used as an alternative to *B.thuringiensis* in the compositions of the present invention

Likewise, culture supernatant taken from cultures of *Xenorhabdus* species, preferably, *X.nematophilus* may be used in place of cells from *Xenorhabdus* species.

Such compositions can be employed, *inter alia*, for crop protection eg. by spraying crops, or for livestock protection. In addition, compositions of the invention may be used in vector control.

The invention further encompasses novel pesticidal agents which can be isolated from *Xenorhabdus spp.* Techniques for isolating such agents would be understood by the skilled person.

In particular, such techniques include the separation and identification of toxin proteins either at the protein level or at the DNA level.

The applicants have cloned and partially sequenced a region of DNA from *Xenorhabdus* NCIMB 40887 which region codes for insecticidal activity and this is shown as Figure 2 (SEQ ID NO. 1) hereinafter. Thus in a preferred embodiment the invention also provides a toxin which is encoded by DNA of SEQ ID No. 1 or a variant or fragment thereof.

The invention also provides a recombinant DNA which encodes such a toxin. The recombinant DNA of the invention may comprise the sequence of Figure 2 or a variant or fragment thereof. Other DNA sequences may encode similar proteins as a result of the degeneracy of the genetic code. All such sequences are encompassed by the invention.

The sequence provided herein is sufficient to allow probes to be produced which can be used to identify and subsequently to extract DNA of toxin genes. This DNA may then be cloned into vectors and host cells as is understood in the art.

DNA which comprises or hybridises with the sequence of Figure 2 under stringent conditions forms a further aspect of the invention.

The expression ``hybridises with'' means that the nucleotide sequence will anneal to all or part of the sequence of Figure 2 under stringent hybridisation conditions, for example those illustrated in ``Molecular Cloning'', A Laboratory Manual'' by Sambrook, Fritsch and Maniatis, Cold Spring Habor Laboratory Press, Cold Spring Harbor, N.Y.

The length of the sequence used in any particular analytical technique will depend upon the nature of the technique, the degree of complementarity of the sequence, the nature of the sequence and particularly the GC content of the probe or primer and the particular hybridisation conditions employed. Under high stringency, only sequences which are completely complementary will bind but under low stringency conditions, sequences which are 60% homologous to the target sequence, more suitably 80% homologous, will bind. Both high and low stringency conditions are encompassed by the term ``stringent conditions'' used herein.

Suitable fragments of the DNA of Figure 2, i.e. those which encode pesticidal agents may be identified using standard techniques. For example, transposon mutagenesis techniques may be used, for example as described by H.S. Siefert et al., Proc. Natl. Acad. Sci. USA, (1986) 83, 735-739. Vectors such as the cosmid cHRIMI, can be mutated using a variety of transposons and then screened for loss of insectidal activity. In this way regions of DNA encoding proteins responsible for toxic activity can be identified.

For example, the mini-transposon mTn3(HIS3) can be introduced into a toxic *Xenorhabdus* clone such as cHRIM1, hereinafter referred to as `clone 1', by electroporating cHRIM1 DNA into *E.coli* RDP146(pLB101) and mating this strain with *E.coli* RDP146(pOX38), followed by *E. coli* NS2114Sm. The final strain will contain cHRIM1DNA with a single insertion of the transposon mTn3(HIS3). These colonies can be cultured and tested for insecticidal activity as described in Example 8 hereinafter. Restriction mapping or DNA sequencing can be used to identify the insertion point of mTn3(HIS3) and hence the regions of DNA involved in toxicity. Similar approached can be used with other transposons such as Tn5 and mTn5.

Site directed mutagenesis of cHRIM1 as outlined in ``Molecular Cloning, A Laboratory Manual'' by Maniatis, Fritsch and Sambrook, (1982) Cold Spring Harbor, can also be used to test the importance of specific regions of DNA for toxic activity.

Alternatively, subcloning techniques can be used to identify regions of the cloned DNA which code for insecticidal activity. In this method, specific smaller fragments of the DNA are subcloned and the activity determined. To do this, cosmid DNA can be cut with a suitable restriction enzyme and ligated into a compatible

restriction site on a plasmid vector, such as pUC19. The ligation mix can be transformed into *E. coli* and transformed clones selected using a selection marker such as antibiotic resistance, which is coded for on the plasmid vector. Details of these techniques are described for example in Maniatis et al, supra, (see p390-391) and Methods in Molecular Biology, by L.G. Davies, M.D. Dibner and J.F. Battey, Elsevier, (see p222-224).

Individual colonies containing specific cloned fragments can be cultured and tested for activity as described in Example 8 hereinafter. Subclones with insecticidal activity can be further truncated using the same methodology to further identify regions of the DNA coding for activity.

The invention also discloses an isolated pesticidal agent characterised in that the agent is obtainable from cultures of *X. nematophilus* or variants thereof, has oral pesticidal activity against *Pieris brassicae, Pieris rapae* and *Plutella xylostella*, is substantially heat stable to 55°C, is proteinaceous, acts synergistically with *B.thuringiensis* cells as an oral pesticide and is substantially resistant to proteolysis by trypsin and proteinase K.

By 'substantially heat stable to 55°C' is meant that the agent retains some pesticidal activity when tested after heating the agent in suspension to 55°C for 10 minutes, and preferably retains at least 50% of the untreated activity.

By 'substantially resistant to proteolysis' is meant that the agent retains some pesticidal activity when exposed to proteases at 30°C for 2 hours and preferably retains at least 50% of the untreated activity.

By 'acts synergistically' is meant that the activity of the combination of components is greater than one might expect from the use of the components individually. For example, when used in conjunction with *B.thuringiensis* cells as an oral pesticide, the concentration of B. thuringiensis cellular material necessary to give 50% mortality in a P.brassicae when used alone is reduced by at least 80% when it is used in combination the agent at a concentration sufficient to give 25% mortality when the agent is used alone.

It has been found that the activity of the material is retained by 30 kDa cut-off filters but is only partly retained by 100 kDa filters.

Preferably the agent is still further characterised in that the pesticidal activity is lost through treatment at 25°C with sodium dodecyl sulphate (SDS - 0.1% 60 mins) and acetone (50%, 60 mins).

Clearly the characterising properties of the isolated agent described above can be utilised to purify it from, or enrich its concentration in, *Xenorhabdus* species cells and culture medium supernatants. Methods of purifying proteins from heterogenous mixtures are well known in the art (eg. ammonium sulphate precipitation, proteolysis, ultrafiltration with known molecular weight cut-off filters, ion-exchange chromatography, gel filtration, etc.). The oral pesticidal activity provides a convenient method of assaying the level of agent after each stage, or in each sample of eluent. Such methodology does not require inventive endeavour by those skilled in the art.

The invention further discloses oral pesticidal compositions comprising one or more agents as described above. Such compositions preferably further comprise other pesticidal materials from non-*Xenorhabdus* species.

These other materials may be chosen such as to have complementary properties to the agents described above, or act synergistically with it.

Preferably the oral pesticidal composition comprises one or more pesticidal agents as described above in combination with *B. thuringiensis* (or with a toxin derived therefrom, preferably endotoxin).

Recombinant DNA encoding said proteins also forms a further aspect of the invention. The DNA may be incorporated into an expression vector under the influence of suitable control elements such as promoters, enhancers, signal sequences etc. as is understood in the art. These expression vectors form a further aspect of the invention. They may be used to transform a host organism so as to ensure that the organism produces the toxin.

The invention further makes available a host organism comprising a nucleotide sequence coding for a pesticial agent as described above.

Methods of cloning the sequence for a characterised protein into a host organism are well known in the art. For instance the protein may be purified and sequenced: as activity is not required for sequencing, SDS gel electrophoresis followed by blotting of the gel may be used to purify the protein. The protein sequence can be used to generate a nucleotide probe which can itself be used to identify suitable genomic fragments from a *Xenorhabdus* gene library. These fragments can then be inserted via a suitable vector into a host organism which can express the protein. The use of such general methodology is routine and non-inventive to those skilled in the art. Such techniques may be applied to the production of *Xenorhabdus* toxins other than those encoded by the sequence of Figure 2.

It may be desirable to manipulate (eg. mutate) the agent by altering its gene sequence (and hence protein structure) such as to optimise its physical or toxicological properties.

It may also be desirable for the host to be engineered or selected such that it also expresses other proteinaceous pesticidal materials (eg. delta- endotoxin from *B. thuringiensis*). Equally it may be desirable to generate host organisms which express fusion proteins composed of the active portion of the agent plus these other toxicity enhancing materials.

A host may be selected for the purposes of generating large quantities of pesticidal materials for purification e.g. by using *B.thuringiensis* transformed with the agent-coding gene. Preferably however the host is a plant, which would thereby gain improved pest-resistance. Suitable plant vectors, eg. the Ti plasmid from *Agrobacterium tumefaciens*, are well known in the art. Alternatively the host may be selected such as to be directly pathogenic to pests, eg. an insect baculovirus.

The teaching and scope of the present invention embraces all of these host organisms plus the agents, mutated agents or agent-fusion materials which they express.

Thus the invention makes available methods, compositions, agents and organisms having industrially applicable pesticidal activity, being particularly suited to improved crop protection or insect-mediated disease control.

The methods, compositions and agents of the present invention will now be described, by way of illustration only, through reference to the following non-limiting examples and figures. Other embodiments falling within

the scope of the invention will occur to those skilled in the art in the light of these.

FIGURE

Figure 1 shows the variation with time of the growth of *X. nematophilus* ATCC 19061 and activity of cells and supernatants against *P. brassicae* as described in Example 3.

Figure 2 shows the sequence of a major part of a cloned toxin gene from *Xenorhabdus*.

Figure 3 shows a comparison of the restriction maps of cloned toxin genes from two strains of *Xenorhabdus* (clone 1 above and clone 3 below).

EXAMPLES

Example 1 - Use of *X. nematophilus* cells as an oral insecticide

CELL GROWTH: A subculture of *X.nematophilus* (ATCC 19061, Strain 9965 available from the National Collections of Industrial and Marine Bacteria, Aberdeen, Scotland) was used to inoculate 250 ml Erlenmeyer flasks each containing 50 ml of Luria Broth containing 10g tryptone, 5g yeast extract and 5g NaCl per litre. Cultures were grown in the flasks at 27°C for 40hrs on a rotary shaker.

PRODUCTION OF CELL SUSPENSION: Cultures were centrifuged at 5000 x g for 10 mins. The supernatants were discarded and the cell pellets washed once and resuspended in an equal volume of phosphate buffered saline (8g NaCl, 1.44g Na_2HPO_4 and 0.24g of KH_2PO_4 per litre) at pH 7.4.

ACTIVITY OF CELL SUSPENSION TO INSECTS: The bioassays were as follows: *P. brassicae*: The larvae were allowed to feed on an artificial agar-based diet (as described by David and Gardiner (1965) London Nature, 207, 882-883) into which a series of dilutions of cell suspension had been incorporated. The bioassays were performed using a series of 5 doses with a minimum of 25 larvae per dose. Untreated and heat-treated (55°C for 10 minutes) cells were tested. Mortality was recorded after 2 and 4 days with the temperature maintained at 25°C.

	LC50 cells/g diet	
Treatment	2 days	4 days
Untreated	5.9×10^5	9.8×10^4
Treated 55°C	7.1×10^5	1.4×10^5

Aedes aegypti: The larva were exposed to a series of 5 different dilutions of cell suspension in deionised water. The biosassays were performed using 2 doses per dilution of 50 ml cell suspension in 9.5cm plastic cups with 25 second instar larvae per dose. Untreated and heat-treated (55°C or 80°C for 10 minutes) cells were tested. Mortality was recorded after 2 days with the temperature maintained at 25°C.

	LC50 cells/ml
Treatment	2 days
Untreated	5.1×10^6
Treated 55°C	7.4×10^6
Treated 80°C	$> 10^8$

Culex quinquefaciatus: The larvae were exposed to a single concentration cell suspension containing 4×10^7 cells/ml. The biosassays were performed using 2 50 ml cell suspensions in 9.5 cm plastic cups with 25 second instar larvae per cup. Untreated and heat-treated (55°C or 80°C for 10 minutes) cells were tested. Mortality was

recorded after 2 days with the temperature maintained at 25°C.

Treatment	% Mortality 2 days
Untreated	100
Treated 55°C	100
Treated 80°C	0

Thus these results clearly show that cells from *X. nematophilus* are effective as an oral insecticide against a number of insect species (and are particularly potent against *P.brassicae*). The insecticidal activity is not dependent on cell viability (i.e is largely unaffected by heating to 55°C which reduces cell viability by >99.99%) but is much reduced by heating to 80°C, which denatures most proteins.

Example 2 - Use of *X.nematophilus* supernatant as an oral insecticide

CELL GROWTH: Cultures were grown as in Example 1.

PRODUCTION OF SUPERNATANT: Cultures were centrifuged twice at 10000g for 10 mins. The cell pellets were discarded.

ACTIVITY OF SUPERNATANT TO INSECTS: The Bioassay was as follows:
Activity against neonate *P. brassicae* and two day old *Pieris rapae* and *Plutella xylostella* larvae was measured as for *P. brassicae* in Example 1, but using a series of untreated dilutions of supernatant in place of of cell supensions and with mortality being recorded after 4 days only.

Insect species	LC50 (μl supernatant/g diet) 4 days
P. brassicae	22
P. rapae	79
P. xylostella	135

In addition, size-reducing activity (62% reduction in 7 days) against *Mamestra brassicae* was detected in larvae fed on an artificial diet containing *X. nematophilus* supernatant (results not shown).

Thus these results clearly show that the supernatant from *X. nematophilus* culture medium is effective as an oral insecticide against a number of insect species, and are particularly potent against *P. brassicae*.

The heating of supernatants to 55°C for 10 minutes caused a partial loss of activity while 80°C caused complete loss of activity. Activity was also completely lost by treatment with SDS (0.1%w/v for 60 mins) and Acetone (50% v/v for 60 mins) but was unaffected by Triton X-100 (0.1% 60 mins), non-diet P40 (0.1% 60 mins), NaCl (1 M for 60 mins) or cold storage at 4°C or -20°C for 2 weeks. All of these properties are consistent with a proteinaceous agent.

The general mode of action of *X. nematophilus* cells and supernatants i.e. reduction in larval size and death within 2 days at high dosages, and other properties, eg. temperature resistence, appear to be similar suggesting a single agent or type of agent may be responsible for the oral insecticide activity activities of both cells and supernatants.

Example 3 - Timescale for appearance of ingestable insecticidal activity

CELL GROWTH: 1ml of an overnight culture of *X. nematophilus* was used to inoculate an Erlenmeyer flask. Cells were then cultured as in Example 1. Growth was estimated by measuring the optical density at 600 nm.

PRODUCTION OF CELL SUSPENSION AND SUPERNATANTS: These were produced as in Examples 1 and 2.

ACTIVITY OF CELLS AND SUPERNATANTS AGAINST *P. BRASSICAE*: The cell suspension bioassay was carried out as in Example 1, but using a single dose of suspended cells equivalent to 50 μl of broth/g diet and measuring mortality after 2 days. The cell supernatant bioassay was carried out as in Example 2, but using a single dose equivalent to 50 μl supernatant/g diet (i.e. more than twice the LC50) and measuring mortality after 2 days.

The results are shown in Fig. 1. Thus these results clearly show that cells taken from *X. nematophilus* culture medium are highly effective as an oral insecticide against *P. brassicae* after only 5 hours, and supernatants are highly effective after 20 hours. Although some slight cell lysis was observed in the early stages of growth, no significant cell lysis was observed after this point demonstrating that the supernatant activity may be due to an authentic extracellular agent (as opposed to one released only after cell breakdown).

Example 4 - Synergy between *X. nematophilus* cells and *B.thuringiensis* powder preparations

CELL GROWTH AND SUSPENSION: *X. nematophilus* cells were grown and suspended as in Example 1. *B. thuringiensis* strain HD1 (from *Bacillus* Genetic Stock Centre, The Ohio State University, Columbus, Ohio 43210, USA) was cultured, harvested and formulated into a powder as described by Dulmage *et al.*(1970) J. Invertebrate Pathology 15, 15-20.

ACTIVITY OF *X. NEMATOPHILUS* CELLS AND *B. THURINGIENSIS* POWDER AGAINST *P. BRASSICAE*: The bioassays was carried out using *X. nematophilus* and *B. thuringiensis* in combination or using *B. thuringiensis* cell powder alone. Bioassays were carried out as in Example 1 but with various dilutions of *B. thuringiensis* powder in place of *X. nematophilus*. For the combination experiment, a constant dose of *X. nematophilus* cell suspension sufficient to give 25% mortaility was also added to the diet. Mortality was recorded after 2 days.

Bioassay	LC50 (μg Bt powder/g diet) 2 days
B.t. alone	1.7
B.t. plus *X.nematophilus*	0.09

These results clearly demonstrate the synergism between *X. nematophilus* cells and *B. thuringiensis* powder when acting as an oral insecticide against *P. brassicae*.

Example 5 - Synergy between of *X.nematophilus* supernatants and *B. thuringiensis* powder

CELL GROWTH AND PRODUCTION OF SUPERNATANTS: *X. nematophilus* cells were grown and supernatants prepared as in Example 2. *B. thuringiensis* was grown and treated as in Example 4.

ACTIVITY OF *X. NEMATOPHILUS* SUPERNATANTS AND Bt CELL POWDER AGAINST *P. BRASSICAE*:
The bioassays were carried out using *X. nematophilus* supernatants and *B. thuringiensis* in combination or using *B. thuringiensis* powder alone. The Bioassay against neonate *P. brassicae* and two day old *Pieris rapae* and *Plutella xylostella* larvae were measured as in Example 2 but with various dilutions of *B. thuringiensis* in place of *X. nematophilus*. For the combination experiment, a

constant dose of *X. nematophilus* supernatant sufficient to give 25% mortality was also added to the diet. Mortality was recorded after 4 days.

	LC_{50} (μg Bt powder/g) diet	
Insect species	Bt alone	Bt plus Xn
P. brassicae	1.4	0.12
P. rapae	2.5	0.26
P. xylostella	7.2	0.63

These results clearly demonstrate the synergism between *X.nematophilus* supernatants and *B.thuringiensis* powder when acting as an oral insecticide against several insect species. The fact that both *X. nematophilus* cells and supernatants demonstrate this synergism strongly suggests that a single agent or type of agent is responsible for the demonstrated activities.

Example 5 - Characterisation of insecticidal agent from *X.nematophilus* supernatant by proteolysis

CELL GROWTH AND PRODUCTION OF SUPERNATANTS: *X. nematophilus* cells were grown and supernatants prepared as in Example 2.

PROTEOLYSIS OF SUPERNATANT: Culture supernatant (50ml) was dialysed against 0.5 M NaCl (3 x 1 l) for 48 hours at 4°C. The volume of the supernatant in the dialysis tube was reduced five-fold by covering with polyethylene glycol 8000 (Sigma chemicals). Samples were removed and treated with either trypsin (Sigma T8253 = 10,000 units/mg) or proteinase K (Sigma P0390 = 10 units/mg) at a concentration of 0.1 mg protease/ml sample for 2 hours at 30°C.

ACTIVITY OF PROTEASE TREATED SUPERNATANT AGAINST *P. BRASSICAE*: The boassay against neonate *P. brassicae*

larvae was carried out by spreading 25 μl of each 'treatment' on the artificial agar-based diet referred to in Example 1 in a 4.5 cm diameter plastic pot. Four pots each containing 10 larvae were used for each treatment. Mortalities were recorded after 1 and 2 days. Controls using water only, trypsin (0.1 mg/ml) and proteinase K (0.1 mg/ml) were also tested in the same way.

	% Mortality	
Treatment	1 day	2 days
Untreated supernatant	60	100
Proteinase K treated supernatant	45	100
Trypsin treated supernatant	40	100
All controls (no supernatant)	0	0

Example 6

Entomocidal activity of other *Xenorhabdus*

Using the methodology of Examples 1 and 2, four different *xenorhabdus* strains were tested against insect pests. The results obtained were as follows:

I) Activity to *Pieris brassicae*

Strain deposit no/code	Cells 10^6/grm diet % mortality	Supernatant LC50 μl/gram of diet
NCIMB 40887	100	0.09
0014	100	0.52
0015	80	3.73
NCIMB 40886	100	0.05

It was found that entomocidal activity of cells and supernatant was reduced by more than 99% when all four strains were heated at 80°C for 10 minutes.

II) Activity to mosquitoes (*Aedes aegypti*)
Bacteria added at the rate of 10^7cells/ml of water

Strain deposit no/code	Cells 10^6/grm diet % mortality
NCIMB 40887	0
0014	40
0015	45
NCIMB 40886	95

Furthermore, all strains significantly reduced the growth of *Heliothis virescens*.

<u>Example 7</u>

<u>Cloning of toxin genes from strains of *Xenorhabdus*</u>

Total cellular DNA was isolated from NCIMB 40887 and ATCC 19061 using a Quiagen genomic purification DNA kit. Cells were grown in L borth (10g tryptone, 5g yeast extract and 5g NaCl per l) at 28°C with shaking (150rpm) to an optical density of 1.5 A_{600}. Cultures were harvested by centrifugation at 4000xg and resuspended in 3.5mls of buffer B1 (50mM Tris/HCl, 0.05% Tween 20, 0.5% Triton X-100, pH7.0) and incubated for 30 mins at 50°C. DNA was isolated from bacterial lysates using Quiagen 100/G tips as per manufacturers instructions. The resulting purified DNA was stored at -20°C in TE buffer (10mM Tris, 1mM EDTA, pH 8.0).

A representative DNA library was produced using total DNA of NCIMB 40887 and ATTC 19061 partially digested with the restriction enzyme *Sau3a*. Approximately 20µg of DNA from each strain was incubated at 37°C with 0.25 units of the enzyme. At time intervals of 10, 20, 30, 45 and 60 minutes, samples were withdrawn and heated at 65°C for 15 minutes. To visualise the size of the DNA fragments, the samples were electrophoresed on 0.5% w/v agarose gels.

The DNA samples which contained the highest proportion of 30 to 50kb fragments were combined and treated with 4 units of shrimp alkaline phosphatase (Boehringer) for 15 minutes at 37°C, followed by heat treatment at 65°C to inactivate the phosphatase.

The size selected DNA fragments were ligated into the BamH1 site of the cosmid vector SuperCos! (Stratagent) and packaged into the *Escherichia coli* strain XL Blue 1, using a Gigapack II packaging kit (Stratgene) in accordance with the manufacturers instructions.

To select for cosmid clones with entomocidal activity, individual colonies selected on L agar plates containing 25μg/ml ampicillin, were grown in L broth (containing 25μg/ml ampicillin) overnight at 28°C. Broth cultures (50μl) were individually spread onto the surface of insect diet contained in 4.5cm diameter pots, as described in Example 5. To each container 10 neonate *P. brassicae* larvae were added. Larvae were examined after 24, 72 and 96 hours recording mortality and size of surviving larvae. A total of 220 clones of NCIMB 40887 were tested, of which two were found to cause reduction in larval growth and death within 72 hours. Of 370 clones from ATTC 19061, one was found to cause larval death within 72 hours.

Example 8

<u>Activity of cloned toxin genes to *Pieris brassicae*</u>

The three active clones from Example 7 were grown in L broth, containing 25μg/ml ampicillin, for 24 hours at 28°C, on a rotary shaker at 150rpm. The activity of the toxin clones to neonate larvae were performed by incorporation of whole broth cultures into insect diet, as described in Example 1.

Clone No	Strain	LC50 (µl broth/g insect diet)
1	NCIMB 40887	13.03
2	NCIMB 40887	16.7
3	ATTC 19061	108.7
Control*		No effect at 100µl/g

*XL1 Blue *E. coli* broth

When *E. coli* toxin clones were heated at 80°C for 10 minutes and added to the diet at a rate of 100µl/g, no activity to larvae was detected. Highlighting the heat sensitivity of the toxins.

Example 9

Sequencing of the cloned toxin from NCIMB 40887

Cosmid DNA of the entomocidal clone 1 above from NCIMB 40887 was purified using the Wizard Plus SV DNA system (Promega) in accordance with the manufacturers instructions. A partial map of the cloned fragment was obtained using a range of restriction enzymes *Eco*R1, *Bam*H1, *Hind*III, *Sal*1 and *Sac*1 as shown in Figure 3. DNA sequencing was intiatiated from pUC18 and pUC19 based sub-clones of the cosmid, using the enzymes *Eco*R1, *Bam*H1, *Hind*III, *Eco*RV and *Pvu*II. Sequence gaps were filled using a primer walking approach on purified cosmid DNA. Sequence reactions were performed using the ABI PRISM™ Dye Terminator Cycle Sequencing Ready Reaction Kit with AmmpliTaq DNA polymerase FS according to the manufacturers instructions. The samples were analysed on an ABI automated sequencer according to the manufacturers instructions. The major part of the DNA sequence for the cloned toxin fragment is shown in Figure 2.

Example 10

Restriction map of cloned toxin from clone 3

Cosmid DNA of the entomocidal clone 3 above was purified as described in Example 9. A restriction map of the cloned fragment was obtained using the restriction enzymes *Bam*H1, *Hind*III, *Sal*1 and *Sac*1 and this is shown in Figure 3. When compared with the map from clone 1 (Figure 3) it is clear that over the regions which overlap, the restriction maps are very similar. The only detectable difference between the two clones was a reduction in size of two *Hind*III fragments in clone 3, corresponding to the 11.4kb and 7.2kb *Hind*III fragments in clone 1 by approximately 2Kb and 200bp respectively. These results indicate the overall relatedness of the DNA region coding for toxicity in the two bacterial strains.

Example 11

Southern Blot Hybridisation Experiments

A 10.3kb *Bam*H1-*Sal*1 fragment of the DNA from clone 1 was used as a probe to hybidise to total *Hind*III digested DNA of the *Xenorhabdus* strains ATCC 19061, NCIMB 40886 and NCIMB 40887. Hybridisation was performed with 20ng/ml of DIG labelled DNA probe at 65°C for 18 hours. Filters were washed prior to immunological detection twice for 5 minutes with 2 x SSC (0.3M NaCl, 30mM sodium citrate, pH 7.0)/0.1% (w/v) sodium dodecyl sulphate at room temperature, and twice for 15 minutes with 0.1 x SSC (15mM NaClm 1.5 mM sodium citrate, pH 7.0) plus 0.1% sodium dodecyl sulphate at 65°C. The probe was labelled and experiments performed in accordance with manufacturers instructions, using a non-radioactive DIG DNA labelling and detection kit (Boehringer). The probe hybridised to a *Hind*III fragment of approximately 8kb in all three strains as well as an 11.4kb fragment in NCIMB 40887 and an approximate 9kb fragment in both NCIMB 40886 and ATCC 19061. These results show that strains NCIMB

40886 and ATCC 19061 contain DNA with close homology to the toxin gene of clone 1 above, confirming the similarity between the toxins produced by the three strains.

ARTICLE 34

CLAIMS:

1. An insecticidal composition which:
(i) is adapted for oral administration to an insect,
(ii) comprises a proteinaceous pesticidal material obtainable from a *Xenorhabdus* species, or a pesticidal fragment thereof, or a pesticidal variant or derivative of either of these,
having in each case toxic activity when administered orally.

2. A composition according to claim 1 wherein the said pesticidal material comprises material encoded by the nucleotide sequence of Figure 2 or variant or fragment thereof, or a sequence which hybridises with said sequence.

3. A composition according to claim 1 or claim 2 which comprises cells of *Xenorhabdus*.

4. A composition as claimed in any one of the preceding claims which comprises supernatant taken from cultures of cells of *Xenorhabdus* species.

5. A composition according to any one of the preceding claims wherein the *Xenorhabdus* species is *Xenorhabdus nematophilus*.

6. A composition according to any one of claims 1 to 4 wherein the *Xenorhabdus* species is ATCC 19061, NCIMB 40886 or NCIMB 40887.

7. A composition as claimed in any one of the preceding claims which comprises a further pesticidal material not obtainable from *Xenorhabdus*.

8. A composition according to claim 7 wherein the said further pesticidal material comprises a material obtainable from *B. thuringiensis*.

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9. A composition according to claim 8 which further comprises cells of *B. thuringiensis*.

10. A composition according to claim 8 wherein the pesticidal materials obtainable from *B.thuringiensis* comprises the delta endotoxin.

11. A composition according to any one of the preceding claims which further comprises an agriculturally acceptable carrier.

12. A composition according to claim 10 wherein the carrier comprises items of insect diet.

13. A method for killing or controlling insect pests, which method comprises administering to a pest or the environment thereof a composition according to any one of the preceding claims.

14. A method as claimed in claim 12 wherein the pests are insects from the order Lepidoptera or Diptera.

15. A microorganism comprising *Xenorhabdus* strain NCIMB 40886.

16. A microorganism comprising *Xenorhabdus* strain NCIMB 40887.

17. A pesticidal agent which comprises a a toxin comprising a protein which is encoded by DNA which includes SEQ ID No. 1 or a variant or fragment thereof.

18. An isolated pesticidal agent characterised in that it is obtainable from cultures of *X. nematophilus* or mutants thereof, has oral pesticidal activity against *Pieris brassicae*, *Pieris rapae* and *Plutella xylostella*, is substantially heat stable to 55°C, is proteinaceous, acts synergistically with *B. thuringiensis* cells as an

oral pesticide, and is substantially resistant to proteolysis by trypsin and proteinase K.

19. An isolated pesticidal agent as claimed in claim 18 further characterised in that the pesticidal activity is substantially destroyed by treatment with sodium dodecyl sulphate or acetone or heating to 80°C.

20. An isolated pesticidal agent as claimed in claim 18 or claim 19 further characterised in that the agent is an extracellular protein.

21. A recombinant DNA which encodes a pesticidal agent according to any one of claims 17 to 20.

22. A recombinant DNA of claim 21 which comprises the sequence of Figure 2 or a variant or fragment thereof.

23. A recombinant DNA which comprises or hybridises under stringent conditions with all or part of the sequence of Figure 2, and which encodes a pesticidal material.

24. An expression vector comprising a recombinant DNA according to any one of claims 21 to 23.

25. A host organism which has been transformed with an expression vector according to claim 24.

26. A host organism as claimed in claim 25 which has been engineered or selected such that it also expresses other pesticidal proteinaceous toxicity enhancing materials

27. A host organism comprising a nucleotide sequence coding for a fusion protein comprising a pesticidally active portion of an agent as claimed in any one of claims 17 to 20 in combination with other pesticidal proteinaceous toxicity enhancing materials.

ARTICLE 34

28. A host organism as claimed in claim 27 wherein the pesticidal toxicity enhancing materials comprise delta-endotoxin from B. thuringiensis.

29. A host organism as claimed in any one of claims 25 to 28 wherein the host is a plant.

30. A host organism as claimed in any one of claims 25 to 28 wherein the host is a virus pathogenic to insects.

31. A fusion protein as expressed by a host as claimed in claim 27.

32. A pesticidal composition comprising one or more agents as claimed in any one of claims 17 to 20.

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Fig.1.

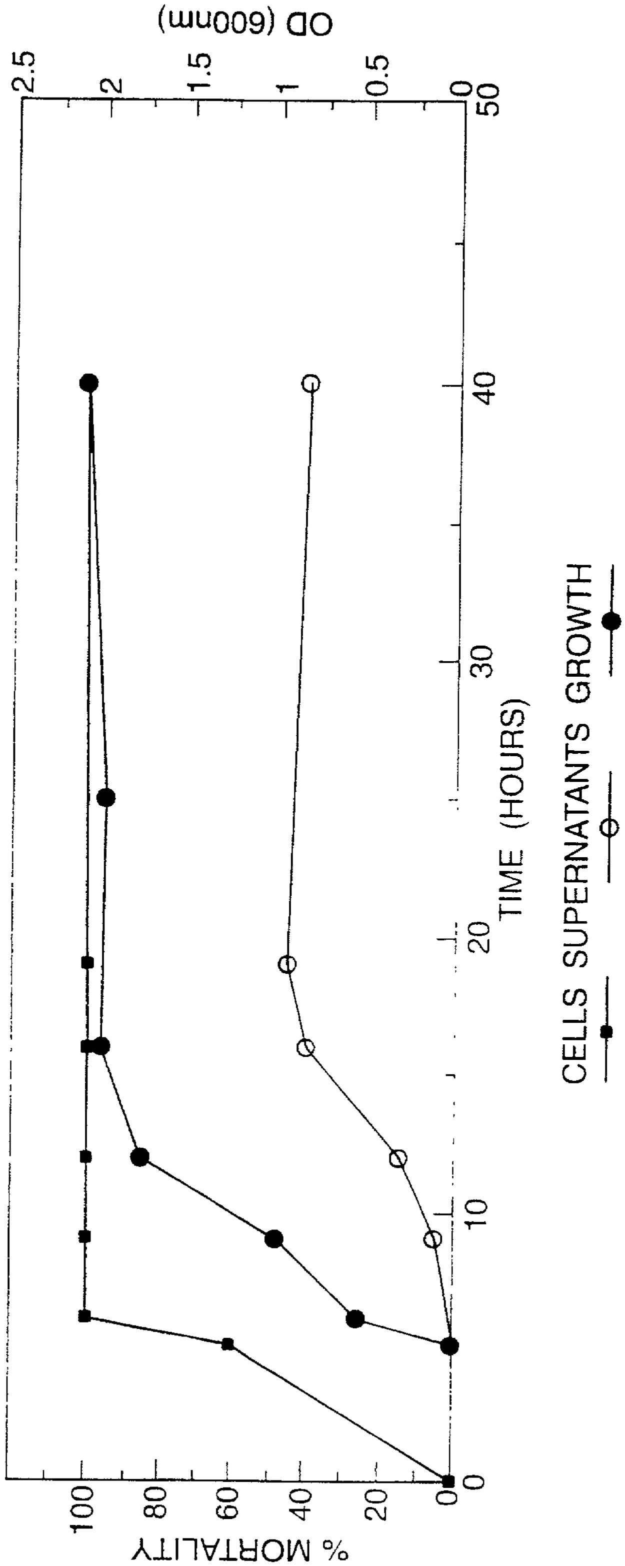
OD (600nm)
2.5
2
1.5
1
0.5
0
% MORTALITY
100
80
60
40
20
0
0
10
20
30
40
50
TIME (HOURS)
CELLS
SUPERNATANTS
GROWTH

Fig.2.

1	TCCACAATTG	CCGGAGAAAA	TCAGTCGGGA	ACTGCCGGTG	ATTATTCGTC	ACTTATTAAA
61	CGAATTTGCC	GACCAGAATA	AGGCTAAAAA	ACTGCTACAG	GCGCAACGCG	ACTCGAACGA
121	AGCGTTAACG	GTAAAGAGTC	ATTCGGATCC	GCTGTATCGC	TTTTGTGGTT	ATCTGGTGTC
181	TGTCAATGAT	ATGACCGGAA	TGAAGATGGG	CAATAAAAAC	ATTAGCCCAC	GAGCACCGAG
241	ATTGTACTTG	TATCATGCCT	ATCTCTCTTT	TATGGAAGCG	CACGGCTTTG	AACGTCCGTT
301	AACACTGACT	AAGTTTGGTG	AATCCATCCC	CAAGATTATG	CTGGAATACC	GGAAGGAGTA
361	TCGAAAAGTG	CGAACCAAGA	AAGGCTATTC	CTATAACGTG	GAATTATCGG	AAGAGGCCGA
421	AGAATGGCTA	CCGTCAGTGC	CTGAGTGTCG	AGACTTTAAA	TCACCTGTAT	AAAACTTTGA
481	GCTTTAAGTC	TGCACTCCAT	ACACAACTTA	AAATATCTAA	TTGTATTTAA	AAGAAAATAA
541	TAGATGTATA	GTTATTTTTT	AACTATACAT	AAGCTCTACA	TGCTCTTCAT	TCGTGTAAAA
601	AATGGGTGAA	CAGGTGATAC	AGTCAGTGAA	TATCATATTA	ATTACCGTAA	ACCCAGATGT
661	AGCAAGGCTT	TCAGGGAATT	GTGCAGAGGG	TGCATAACTG	AGAGGGTGAA	AAAGATTTTC
721	AGGGGGGCTT	ATGGCAGGTA	AACAAAATCA	GAAGCAAATA	CCGTGCACAA	TCTGGTTTTT
781	ATTTTTTGGT	ACTACCTCAA	ATTAAAATGA	TGTAATCATC	TGATTTTATT	TAAGAATAGA
841	AGTTAATCAC	AATTTCATTG	ATGGACTTTC	ATTCACACTG	GTATAGATAA	ATAATTCTGT
901	TATATCCTGT	TTCATTACGC	ATTCATCAGG	AGTGCTGTTA	CAGGAGACAA	GAATGTCACA
961	CATCATTTAC	TTGTCGTTAA	AGGGCAAGAA	GCAGGGTTTA	ATTTCAGCGG	GTTGTTCAAC
1021	GCCTGAATCA	ATTGGAAATC	GCTATCAAAA	AGGACGTGAA	GATCAAATAC	AGGTATTGAG
1081	CCTGAATCAT	TCGATGAGCC	GTGACCAGAA	TGTTAATCAT	CAACCCGTCA	GTTTTGTGAA
1141	ACCCATTGAT	AAATCCTCTC	CCCTGTTTGC	TGGATGCCAG	TTTTGTGCAT	TACAGGACAA
1201	GCCAGATGGG	ACAACTGGAG	TTCTTTTATG	AAATCAAGCT	GACCAGTGCC	ACGATTGTGG
1261	ATATTTCCTA	TAATTATCCG	GCATTCAATC	AATGATAATG	GTGCGATACC	CCATGAAGTG
1321	GTGATGCTCG	ATTATAAGTC	CATTTCATGC	AACCACATCG	CCGCAGGACT	TCGGGCTACA
1381	GCATACGCAA	TTAGCCGGAA	GTGAAGAAGC	AAGCCGCTTT	TATCTGGGGT	CTCGAATGTT
1441	AAGCCACTTA	AGAAGCCGCT	GGTTGAAGAA	ACCCCGGTAA	AACCCGCTAA	ACATCATGCC
1501	CGTTATCGTT	GTGTGGATGA	TGACGGCAAT	CTTTTAACCG	AACGCAAGTA	TCGGGTTTGC
1561	CTGCCGGATG	GTCAGATAAA	AGAAGGAAAG	ACTGATAAAC	AAGGTTACAC	CCAATGGCAT
1621	CTTACGGATG	ACAAAAATAA	ACTTGAATTT	CATATTTTAA	AGGATTAATA	CCATGCCAGC
1681	CTATACCGTT	CAGACAAAAA	TAGAATCCAA	CGTACCTGTT	GAAAACCTGC	TTTACGACTT
1741	AACCATTTAT	CGTAAGGATG	CAAAAGGAAA	TTTCCATATC	TTGCTTGATG	TTTTTCAGGA
1801	GAAACTACAG	AGTAATTATG	AAACACAACA	GCATATCACG	CAGGAAATAG	ACGACGATCT
1861	TTCTGTGATT	TATATTATGC	AAATTATGCT	TCACCGCAAA	CATGGCTCAA	ATATATTTCC
1921	GGCACTGCAA	ACCCATTTTA	AGAAAATGTA	TACCCTCGGT	GAATTAACTT	CCGGTAAAGC
1981	CTGTTCGGAG	AAAAAACGGG	AAAATGCCTG	TTATTTTGAA	AGTACAGTTG	AAACAAAACC
2041	TGTCAGCGAC	GGGGATAATA	CCGTTGACTT	AAATATCACT	ATTCCTGAAC	GACCTTTTAT
2101	TGCCAAAGAA	TATCCCATTG	GTCACCCACA	CGATCCATTT	GAAAAAAGTA	AAATTGAATC
2161	ATAAATACAG	GACAGGTTAT	CGAAAAGAAT	TTATCCGGAT	CAAAATGGAG	CAAGTTTATG
2221	TCAGGGCGCG	AGCACACTAT	TTTAGCTGCG	TTTTTAAGAT	GATTATCTCT	TAATGTTCAG
2281	TTTTAATAGT	GTTTTTATCG	AGTGAAATTT	AATCGCACAG	GCAATTCTTT	AGACTTTTAT
2341	AGAAAACTAA	AGAATTAAAG	AACAAGATTG	ACATTTTAAG	TTCAAATATT	AATCAAAGTA
2401	TGCTCGCGCC	CTGAGTTTAT	GTGGCCCTGC	CGCTTTTTTT	TATTGCCTGC	CAATAGATAG
2461	ACCAGATATT	TATGAGCAAG	CGGCACGAGA	ATTATGGCAA	TATGGCCGAA	CTAAAATTGG
2521	TCAACTGGAA	ATTAAGCCGG	GTGAGGGTTG	CCGACATCCT	AAAGGTACTT	TTTATAATCA
2581	ATATGGTGAA	AGAATATCTG	GGTTAGATTG	GCTGACATTG	GCAAGCCTAA	GAGATTCAGA
2641	AAATATGATG	ATGAGGTTGA	TGATGAAGTA	GCTGGTATTA	CAATGTGGGG	AAAATTGACA
2701	GAATGGTTTG	AAAAATCAGG	GTATGAAAAA	GTATTTAGTA	ATGTCGGCTT	ATCCCATTCT
2761	AATATAAATG	ACATAGTAAC	TCTTAGTGAT	TACTATAACA	AAGGATATCA	TGTTGTTACT
2821	TTGATTTCAG	CAGGAATGTT	ATCAGATTTT	GGTGACATAG	AAACATCAGG	AAAAAATCAT
2881	TGGATAGTTT	GGGAAGGAGT	AGTAGAAAAC	TATGAGAAAG	AAAATATCAC	AAATAATTCA
2941	GATCTGAATC	AATATGTAAA	TTTAAATCTG	TTTTCATGGG	GTAAAGTGGA	ACATCAAATT
3001	AAAAAAAACA	AATCACTAGA	TTATGTACTC	AACCATATTT	TTTGAGGGTT	GGTTTTTAAA
3061	CCAATGAAAT	AACATGAAAA	AAATATTAAT	TATTTTTATT	TTTTTACTTT	ATGGTTGTGG
3121	TAATCCAACG	CCAAAAGTTT	TACCAAAATC	AGAGTTTCTT	CCTGATGCAG	TGATAAATGA
3181	ACCATATCAG	GCATCAATTA	CCATCACAGG	AGGTGCATTG	AATGAAAAAA	GCGTTTGGGT
3241	AAAAATTCAT	CCTACTGGCT	CAGGACTAAC	ATGGAATCCA	AAAGATAGTT	CTTTCCTATA
3301	GGGTGGAAAA	AAAGAAATAA	GAAAAGATTA	TCATCATATA	AATATAACAG	GTACCCCAAA
3361	GAAGACAGAA	TTGATAAAAA	TTGAAGTGGT	AGGATTTACA	TTGGGTACAA	TGTACGCACG
3421	GAAAGAGTTC	ACTATAAATT	ATACTATAAA	AGTAAGGGAA	TAATTGTCAC	TATCAGAATG
3481	GTGATTTAAT	TCGCCATTTT	TATACTTTTG	TATACTCTCT	CAACATAATC	AGGATTCTTT

Fig.2.

```
3541  CTTATTATTT TTCATGGTGC TAAAAACGTT TATTGCAAAA ATAAATTAAG TTAATCAGAT
3601  AAATTATCTG CATTACTGTT ATAATCGATA ACACGATAAC CTGACTTTCT GCCTGTTCTT
3661  ATGAACTCGA AGATAATCCT TTCTGAGCCT GAACGAATCA CATTGCAACC ACTCGCTTTG
3721  AATCACCCAC ACCGGGACAT TCGTACGCGA GGAACGGGTT TACTCATGCT TGCCAGAGGG
3781  AGCAAGCCGT CCCAGATCAC CGCTGAAATC GGATGCAGTC TCCGGGTTAT CTGTAATTGG
3841  GTTCACATGT GGCACAGATA GCGGGATTAT TCGGCGGTCA TGCCGGAGGC CGGTATCTCG
3901  CCATGACGCC TGACATGATT GCCACTGCGC TCGAAGCCGC CAGCGCAGAG TCCCTGACGT
3961  GCGTCGAAGC CAGGCAGGGT TTCCCTGCCT TGTACGCTTG AAACGCTGGC GAATACCCTG
4021  AAAAAACAGG GGCTCCCCTA TAAACGCCCC CGCCTGTCGC TTAAAAAAAG CGCAATAAAA
4081  CGGAGTTTGC TGAAAAATCC GCCTTGCTGA ATAAAATTAA GGCCGGAGCA CAGTCAGGAC
4141  ATTACCGTCT GGTCTATTTT GAGTTCTGGG GGCGTTAAAT TACACGGATA ACACGCTGTT
4201  TTACCAGACA ACGTCAGGCA GTATCACGCG AGATGACGTG ATTGATTTTT TAGAGCCGGT
4261  GGCCAGACAA GGGACAACCG CCTGACATTT TTAGTGTTGG ATAATGCGCG TATCCATCAC
4321  GGGATAGAGG AAAAAATCAG AAATGGCGGG TGACGAGAAC ACAACCTGTT TTTATTCTAT
4381  CTTCCCGCTT ACAGCCCAGA GCTGTATCTG ATTGAAATCG TCTGGAAACA GGCCAAATAC
4441  GACTGGCGAC GTTTTATCAC CTGGACTCAG GATACAATGG AATATGAGGT AAATACTTTA
4501  TTGAAAGGTT ATGGCGACCA ATTTGCAATT AACTTTTCTT GAGTACTTAG TAAGAATAGA
4561  GTCAGTCGAG GTTTTTTCAT TTCGGGTCGT GGGGATGATA CTGAAAATTT GTTTGTAATC
4621  TCTGAAAATT GCTGTTTCTG TGGCTACGTC TGTCTTTTGG GATATTGTTT CCATCAAGTC
4681  TGTCAACATA CTGTTAAGTT AGATGTTGAT AAAAGAGACT GAATTATAAT ACAAAACAAT
4741  AAATCACTTG GACAATATTT TATTTCACAT GAGACATTAA GGTTGATTTT CCCAATCTGG
4801  TCAGTTATAA CCGAATAAGG ATCTTGAAAA ATCATGGGAT CTTACTTTTA TCAAATGAAG
4861  TTAACGTAAA AGTTGATAAA GAAAATTATT TAATTCTAAG TGCCGTTGGC ATAAATATTT
4921  TGTGTTTTGT TAATGAATGA ATAACCAGGT AAGCTGGATT TTCATTTTTT AATTACTCGT
4981  TACAATATGC TATTTATTTA TATAAAGAGT TTGTGCCCAT TTAACCAGTA AACAAATTTG
5041  TTCAACCGTA ACTTAGCTTC ATCGACTTTT GGCCTCGCCT GGTCAGAATC TAGGGCCGTT
5101  ATCCTATTTA TTTATGATAA ATAAAATTTA ATTATCTTTA ATAAGCTGAA TATGTGGATT
5161  TGTGCTCAAT CTTGGATTCA AGTATGTATT CCTTTTGGTA CCCTGCTTTA TTTTAAGGCA
5221  GATGAAGAGG ATGCCAACAT GACACAATAT CGATTACGAC TGTAACATTA AAGTCAGTTA
5281  TAAATTTTAT GATTAAAATG AAATTTTAGT AGAAAATCGT ATTCTATTCC GCCATTTACA
5341  ATAGCATCCT CTTTAATATC ATTAATCTCA GATAAAACAA ATAATTACAA TGTGAATAGA
5401  ATAATGACTT ACAAAATAAG CACTAAATCT TCAGATGAAC TCTTAACTGA CAACACTATT
5461  TTATAAAATA ATTGAGGTTA TTATGTATAG CACGGCTGTA TTACTCAATA AAATCAGTCC
5521  CACTCGCGAC GGTCAGACGA TGACTCTTGC GGATCTGCAA TATTTATCCT TCAGTGAACT
5581  GAGAAAAATC TTTGATGACC AGCTCAGTTG GGGAGAGGCT CGCCATCTCT ATCATGAAAC
5641  TATAGAGCAG AAAAAAAATA ATCGCTTGCT GGAAGCGCGT ATTTTTACCC GTGCCAACCC
5701  ACAATTATCC GGTGCTATCC GACTCGGTAT TGAACGAGAC AGCGTTTCAC GCAGTTATGA
5761  TGAAATGTTT GGTGCCCGTT CTTCTTCCTT TGTGAAACCG GGTTCAGTGG CTTCCATGTT
5821  TTCACCGGCT GGCTATCTCA CCGAATTGTA TCGTGAAGCG AAGGACTTAC ATTTTTCAAG
5881  CTCTGCTTAT CATCTTGATA ATCGCCGTCC GGATCTGGCT GATCTGACTC TGAGCCAGAG
5941  TAATATGGAT ACAGAAATTT CCACCCTGAC ACTGTCTAAC GAACTGTTGC TGGAGCTATT
6001  ACCCGCAAGA CCGGAGGTGA TTCGGACGCA TTGATGGAGA GCCTGTCAAC TTACCGTCAG
6061  GCCATTGATA CCCCTTACCA TCAGCCTTAC GAGACTATCC GTCAGGTCAT TATGACCCAT
6121  GACAGTACAC TGTCAGCGCT GTCCCGTAAT CCTGAGGTGA TGGGGCAGGC GGAAGGGGCT
6181  TCATTACTGG CGATTCTGGC CAATATTTCT CCAGAACTGT ATAACATTTT GACCGAAGAG
6241  ATTACGGAAA AGAACGCTGA TGCTTTATTT GCGCAAAACT TCAGTGAAAA TATCACGCCC
6301  GAAAATTTCG CGTCACAATC ATGGATAGCC AAGTATTATG GTCTTGAACT TTCTGAGGTG
6361  CAAAAATACC TCGGGATGTT GCAGAATGGC TATTCTGACA GCACCTCTGC TTATGTGGAT
6421  AATATCTCAA CGGGTTTAGT GGTCAATAAT GAAAGTAAAC TCGAAGCTTA CAAAATAACA
6481  CGTGTAAAAA CAGATGATTA TGATAAACAT GTAAATTACT TTGATCTGAT GTATGAAGGA
6541  AATAATCAAT TCTTTATATG TGCTAATTTT AAGATATCGA GAGAATTTGG GGCGACTCTT
6601  AGGAAAAACT CAGGGACAAG TGGCATTGTC GGCAGCCTTT CCGGTCCCCT GGTAGCCAAT
6661  ACTAATTTCA AAAGCAATTA CTTAAGTAAC ATATCTGATA ATGAATACAG AAATGGCGTA
6721  AAAATATATG CCTATCGCTA TACGTCTTCC ACCAGCGCCA CAAATCAGGG CGGCGGAATA
6781  TTCACTTTTG AGTCTTATCC CCTGACTATA TTTGCGCTCA AACTGAATAA AGCCATTCGC
6841  TTGTGCCTGA CTAGCGGGCT TTCACCGAAT GAACTGCAAA CTATCGTACG CAGTGACAAT
6901  GCACAAGGCA TCATCAACGA CTCCGTTCTG ACCAAAGTTT TCTATACTCT GTTCTACAGT
6961  CACCGTTATG CACTGAGCTT TGATGATGCA CAGGTACTGA ACGGATCGGT CATTAATCAA
7021  TATGCCCGAC GATGACAGTG TCAGTCATTT TAACCGTCTC TTTAATACCC CGCCGCTGAA
7081  AGGGAAAATC TTTGAAGCCG ACGGCAACAC GGTCAGCATT GATCCGGATG AAGAACAATC
7141  TACCTTTGCC CGTTCAGCCC TGATGCGTGG TCTGGGGATC AACAGTGGTG AACTGTATCA
7201  GTTAGGCAAA CTGGCGGGTG TATTGGACAC ACAAAATATC CTCACACTTT CTGTCCCTGT
7261  TATATCTTCA CTGTATCGCC TCACGTTACT GGCCCGTGCC CATCAGCTGA CGGTTAATGA
7321  ACTGTGTATG CTTTATGGTT TTTCGCCGTT CAATGGCAAA ACAACGGCTT CTTTGTCTTC
```

Fig.2.

7381	CGGGGAGTTG	TCACGGCTGG	TTATCTGGTT	GTATCAGGTG	ACGCAGTGGC	TGACTGAGGG
7441	CGGAAATCAC	CACTGAAGCG	ATCTGGTTAT	TATGTACGCC	AGAGTTCAGC	GGGAATATTT
7501	CACCGGAAAT	CAGTAATCTG	CTTAATACTC	TCCGACCCCG	TATTAGTGAA	GACATGGCAC
7561	AAAGTAGTGA	CCGGGAGCTT	CAGGCTGAAA	TTCTCGCGCC	GTTTATTGCT	GCAACGCTGC
7621	ATCTGGCGTC	ACCAGATATG	GCGCGGTATA	TCCTGTTGTG	GACTGATAAC	CTGCGGCCGG
7681	GCGGCCTGAA	TATCGCCGGA	TTTATGATGC	TGGTGCTGAA	AGAGACGCTG	AGTGATGAGG
7741	AAACGACCCA	ACTGGTTCAA	TTCTGCCATG	TAATGGCACA	GTTATCGCTT	TCCGTGCAGA
7801	CACTGCGTCT	CAGTGAAGCA	GAGCTTTCTG	TGCTGGTCAT	TTCCGATTTT	GTGGTACTGG
7861	GTGCGAGAAG	CCAACCGCCG	GACAACACAA	TATTGATACT	CTGTTCTCAC	TCTACCGATT
7921	CCACCAGTGG	ATTAATGGGC	TGGGAAATCC	CGGCTCTGAC	ACGCTGGATA	TGCTGCGCCA
7981	AGCAGACACT	CACGGGCGAC	AGACTGGGCC	TCCGTGATGG	GGCTGGACAT	CAGTATGGTA
8041	ACGCAGGCCA	TGGGTTCCCG	CCGGCGTGAA	CCAACTTCAG	TGTTGGCAGG	ATATCAACCC
8101	CGTGTTGCAG	TGGATACATG	TGGCATCAGC	ACTGCTCACT	GATGCCGTCG	GTTATCCGTA
8161	CGCTGGTGAA	TATCCGTTAC	GTGACTGCAT	TAAACAAAGC	CGAGTCGAAT	CTGCCTGCCT
8221	GGGATAAGTG	GCAGACGCTG	GCAGAAAATA	TGGCAGCCGG	ACTGAGTACA	CAACAGGCTC
8281	AGACGCTGGC	GGATTATACC	GCAGAGCGCC	TGAGTAACGT	GTTGTGCAAT	TGGTTTCTGG
8341	CGAATATCCA	GCCAGAAGGG	GTGTCCCTGC	ACAGCCGGGA	TGACCTGTAC	AGCTATTTCC
8401	TGATTGATAA	TCAGGTCTCT	TCTGCCATAA	AAACCACCCG	ACTGGCAGAG	GCCATTGCCG
8461	GTATTCAGCT	CTACATCAAC	CGGGCGCTGA	ACCGGATAGA	GCCTAATGCC	CGTGCCGATG
8521	TGTCAACCCG	CCAGTTTTTT	ACCGACTGGA	CGGTGAATAA	CCGTTACAGC	ACCTGGGGCG
8581	GGGTGTCGCG	GCTGGTTTAT	TATCCGGAAA	ATTACATTGA	CCCGACCCAG	CGTATCGGGC
8641	AGACCCGGAT	GATGGATGAA	CTGCTGGAAG	ATATCAGCCA	GAGTCAGCTC	AGCCGGGACA
8701	CGGTGGAAGA	GGCCTTTAAA	ACTTACCTGA	CCGCTTTGAA	ACCGTGGCAG	ACCTGAAAGT
8761	TGTCAGCGCT	ATCACCGACA	ACGTCAACAG	CAACACCGGA	CTGACCTGGT	TTGTCGGCCA
8821	AACGCGGGAG	AACCTGCCGG	AATATTACTG	GCGTAACGTG	CATATATCAC	GGATGCAGGC
8881	GGGTGAACTG	GCCGCCGATG	CCTGGAAAGA	TTGGACGAAG	ATTGATACAG	CGGTCAACCC
8941	ATACAAGGAT	GCAATACGTC	CGGTCATATT	CAGGGAACGT	TTGCACCTTA	TCGTGGGTAG
9001	AAAAAGAGGA	AGTGGCGAAA	AATGGTACTG	ATCCGGTGGA	AACCTATGAC	CGTTTTACTC
9061	TGAAACTGGC	GTTTCTGCGT	CATGATGGCA	GTTGGAGTGC	CCCCTGGTCT	TACGATATCA
9121	CAACGCAGGT	GGAGGCGGTC	ACTGACAAAA	AACCTGACAC	TGAACGGCTG	GCGCTGGCCG
9181	CATCAGGCTT	TCAGGGCGAG	GATACTCTGC	TGGTGTTTGT	GTACAAAACC	GGGGTGAGTT
9241	ACCCGGATTT	TGGCGACAAC	AATAAAAATG	TGGCAGGCAT	GACCATTTAC	GGCGATGGCT
9301	CCTTCAAAAA	GATGGAGAAC	ACAGCACTCA	GCGTTACAGC	CAACTGAAAA	ATACCTTTGA
9361	TATCATTCAT	ACTCAAGGCA	ACGACTTGGT	AAGAAAGGCC	AGCTATCGTT	TCGCGCAGGA
9421	TTTTGAAGTG	CCTGCCTCGT	TGAATATGGG	TTCTGCCATC	GGTGATGATA	GTCTGACGGT
9481	GATGGAAAAC	GGGAATATTC	CGCAGATAAC	CAGTAAATAC	TCCAGCGATA	ACCTTGCTAT
9541	TACGCTACAT	AACGCCGCTT	TCACTGTCAG	ATATGATGGC	AGTGGCAATG	TCATCAGAAA
9601	CAAACAAATC	AGCGCCATGA	AACTGACGGG	GTTGGATGAA	AGTCCCAGTA	CGGCAATGCA
9661	TTTATCATCG	CAAATACCGT	TAAACATTAT	GGCGGTTACT	CTGATCTGGG	GGGCCCGATC
9721	ACCGTTTTTA	TTAAAACGGA	AAAACTATAT	TGCATCAGTT	CAAGGCCACT	TGATGAACGC
9781	AGATTACACT	AGGCGTTTGA	TTCTAACACC	AGTTGAAAAT	AATTATTATG	CCAGATTGTT
9841	CGAGTTTCCA	TTTTCTCCAA	ACACAATTTT	AAACACCGTT	TTCACGGTTG	GTAGCAATAA
9901	AACCAGTGAT	TTTAAAAAGT	GCAGTTATGC	TGTTGATGGT	AATAATTCTC	AGGGCTTCCA
9961	GATATTTAGT	TCCTATCAAT	CATCCGGCTG	GCTGGATATT	GACACAGGTA	TTAACAATAC
10021	TGATGTCAAA	ATTACGGTGG	TAGCTGGCAG	TAAAACCCAC	ACCTTTACGG	CCAGTGACCA
10081	TATTGCTTCC	TTGCCGGCAA	ACAGTTTTGA	TGCTATGCCG	TACACCTTTA	AGCCACTGGA
10141	AATCGATGCT	TCATCGTTGG	CCTTTACCAA	TAATATTGCT	CCTCTGGATA	TCGTTTTTGA
10201	GACCAAAGCC	AAAGACGGGC	GAGTGCTGGG	TAAGATCAAG	CAAACATTAT	CGGTGAAACG
10261	GGTAAATTAT	AATCCGGAAG	ATATTCTGTT	TCTGCGTGAA	ACTCATTCGG	GTGCCCAATA
10321	TATGCAGCTC	GGGGTGTATC	GTATTCGTCT	TAATACCCTG	CTGGCTTCTC	AACTGGTATC
10381	CAGAGCAAAC	ACGGGCATTG	ATACTATCCT	GACAATGGAA	ACCCAGCGGT	TACCGGAACC
10441	TCCGTTGGGA	GAAGGCTTCT	TTGCCAACTT	TGTTCTGCCT	AAATATGACC	CTGCTGAACA
10501	TGGCGATGAG	CGGTGGTTTA	AAATCCATAT	CGGGAATGTT	GGCGGTAACA	CGGGAAGGCA
10561	GCCTTATTAC	AGCGGAATGT	TATCCGATAC	GTCGGAAACC	AGTATGACAC	TGTTTGTCCC
10621	TTATGCCGAA	GGGTATTACA	TGCATGAAGG	TGTCAGATTG	GGGGTTGGAT	ACCAGAAAAT
10681	TACCTATGAC	AACACTTGGG	AATCTGCTTT	CTTTTATTTT	GATGAGACAA	AACAGCAATT
10741	TGTATTAATT	AACGATGCTG	ATCATGATTC	AGGAATGACG	CAACAGGGGA	TCGTGAAAAA
10801	TATCAAGAAA	TACAAAGGAT	TTTTGAATGT	TTCTATCGCA	ACGGGCTATT	CCGCCCCGAT
10861	GGATTTCAAT	AGTGCCAGCG	CCCTCTATTA	CTGGGAATGT	TCTATTACAC	CCCGATGATG
10921	TGCTTCCAGC	GTTTGCTACA	GGAAAAACAA	TTCGACGAAG	CCACACAATG	GATAAACTAC
10981	GTCTATAATC	CCGCCGGCTA	TATCGTTAAC	GGAGAAATCG	CCCCCTGGAT	CTGGAACTGC
11041	CGGCCGCTGG	AAGAGACACT	CCTGGAATGC	CAATCCGTTG	GATGCCATTG	ATCCGGATGC
11101	CGTCGCACAA	TATGACCCGA	CACACTATAA	AGTTGCCACC	TTTATGCGCC	TGTTGGATCA
11161	ACTTATTCTG	CGCGGCGATA	TGGCCTATCG	CGAACTGACC	CGCGATGCGT	TGAATGAAGC

Fig.2.

11221	CAAGATGTGG	TATGTGCGTG	CTTTGGAATT	GCTGGGTGAT	GAGCCGGAGG	ATTACGGCAG
11281	CCAACAGTGG	GCCGCACCGT	CTCTTTCCGT	GGCGGGCAAC	CACACTGTGC	AAGCGGGCTA
11341	TCAACAAGAC	CTTACGGCGC	TAGACAACGG	AGAAGGTTGC	ACTCAACCCC	GCAACGCTAA
11401	CTCGTTGGTG	GTTTGGTCCT	GCCGGAATAT	AACCCGGAAT	CAACCGATTA	CTGGCAAACC
11461	TGCGTTTGCG	CCTGGTTAAC	CTGCGCCATA	ATCCTTCCAT	GACGGGCAAC	CGTTATCGCT
11521	GGCGAATTAC	GCGAGCCTAC	GATCCGAAAG	CGCTGCTCAC	CAGTATGGTA	CAGCCTTCTC
11581	AGGGCGGTAG	TGCAGTGCTG	CCCGGCACAT	TGTCGTTATA	CCGCTTCCCG	GTGATGCTGG
11641	AGCGGGCCCG	CAATCTGGTA	GCGCAATTAA	CCCAGTTCGG	CACCTCTCTG	CTCAGTATGG
11701	CAGAGCATGA	TGATGCCGAT	GAACTCACCA	CGTTGCTACT	ACAGCAGGGT	ATGGAACTGG
11761	CGACACAGAG	CATCCGTATT	CAGCAACGAA	CTGTCGATGA	AGTGGATGCT	GATATTGCTG
11821	TATTGGCAGA	GAGCCGCCGC	AGTGCACAAA	ATCGTCTGGA	AAAATACCAG	CAGCTGTATG
11881	ACGAGGATAT	CAACCACGGA	GAACAGCGTG	CGATGTCACT	GTTTGATGCG	GCGGCAGGTC
11941	AGTCTCTGGC	CGGGCAGGCG	CTCTCAGTAG	CAGAAGGGGT	GGCTGACTTA	GTTCCAAACG
12001	TGTTCGGTTT	CGCTTGTGGC	GGCAGTCGTT	GGGGGGCAGC	ACTGCGTGCT	TCCGCCTCCG
12061	TGATGTCGCT	TTCTGCCACA	GCTTCCCAAT	ATTCCGCAGA	CAAAATCAGC	CGTTCGGAAG
12121	CCTACCGCCG	CCGCCGTCAG	GAGTGGGAAA	TTCAGCGTGA	TAATGCTGAC	GGTGAAGTCA
12181	AACAAATGGA	TGCCCAGCTG	GAAAGCCTGA	AAATACGCGG	CGAAGCAGCA	CAGATGCAGG
12241	TGGAATATCA	GGAGACCCAG	CAGGCCCATA	CTCAGGCTCA	GTTAGAGCTG	TTACAGCGTA
12301	AATTCACAAA	CAAAGCGCTT	TACAGTTGGA	TGCGCGGCAA	GCTGAGTGCT	ATCTATTACC
12361	AGTTCTTTGA	CCTGACCCAG	TCCTTCTGCC	TGATGGCACA	GGAAGCGCTG	CGCCGCGAGC
12421	TGACCGACAA	CGGTGTTACC	TTTATCCGGG	GTGGGGCCTG	GAACGGTACG	ACTGCGGGTT
12481	TGATGGCGGG	TGAAACGTTG	CTGCTGAATC	TGGCAGAAAT	GGAAAAAGTC	TGGCTGGAGC
12541	GTGATGAGCG	GGCACTGGAA	GTGACCCGTA	CCGTCTCGTT	GGCACAGTTC	TATCAGGCCT
12601	TATCATCAGA	CAACTTTAAT	CTGACCGAAA	AACTCACGCA	ATTCCTGCGT	GAAGGGAAAG
12661	GCAACGTAGG	AGCTTCCGGC	AATGAATTAA	AACTCAGTAA	CCGCCAGATA	GAAGCCTCAG
12721	TGCGATTGTC	TGATTTGAAA	ATTTTCAGCG	ATACCCCGGA	AAGCTTTGGC	AATACCCGTC
12781	AGTTGAAACA	AGTGAGTGTC	ACCTTGCCGG	CGCTGGTTGG	TCCGTATGAA	GATATCCGGG
12841	CGGTGCTGAA	TTACGGCGGC	AGCATCGTCA	TGCCACGCGG	TTGCAGTGCT	ATTGCTCTCT
12901	CCCACGGCGT	GAATGACAGT	GGTCAATTTA	TGCTGGATTT	CAACGATTCC	CGTTATCTGC
12961	CGTTTGAAGG	TATTTCCGTG	AATGACAGCG	GTAGCCTGAC	GTTGAGTTTC	CCGGATGCGA
13021	CTGATCGACA	GAAAGCGCTG	CTGGAGAGCC	TGAGCGATAT	CATTCTGCAT	ATCCGCTATA
13081	CCATTCGTTC	TTAATTAAAA	CATTGTGATA	GGCAGGCTCC	TGAGGGAGCC	TGTTTAAGGA
13141	GTTTTTATGC	AGGGTTCAAC	ACCTTTGAAA	CTTGAAATAC	CGTCATTGCC	CTCTGGGGGC
13201	GGATCACTAA	AAGGAATGGG	AGAAGCACTC	AATGCCGTCG	GAGCGGAAGG	GGAGCGTCAT
13261	TTTCACTGCC	CTTGCCGATC	TCTGTCCGGC	GTGGTCTGGT	GCCGGTGCTA	TCACTGAATT
13321	ACAGCAGTAC	TGCTGGCAAT	GGGTCATTCG	GGATGGGGTG	GCAATGTGGG	GTTGGTTTTA
13381	TCAGCCTGCG	TACCGCCAAG	GGCGTTCCGC	ACTATACGGG	ACAAGATGAG	TATCTCGGGC
13441	CGGATGGGGA	AGTGTTGAGT	ATTGTGCCGG	ACAGCCAAGG	GCAACCAGAG	CAACGCACCG
13501	CAACCTCACT	GTTGGGGACG	GTTCTGACAC	AGCCGCCTAC	TGTTACCCGC	TATCAGTCCC
13561	GCGTGGCAGA	AAAAATCGTT	CGTTTAGAAC	ACTGGCAGCC	ACAGCAGAGA	CGTGAGGAAG
13621	AGACGTCTTT	TTGGGTACTT	TTTACTGCGG	ATGGTTTAGT	GCACCTATTC	GGTAAGCATC
13681	ATCATGCACG	TATTGCTGAC	CCGCAGGATG	AAACCAGAAT	TGCCCGCTGG	CTGATGGAGG
13741	AAACCGTCAC	GCATACCGGG	GAACATATTT	ACTATCACTA	TCGGGCAGAA	GACGATCTTG
13801	ACTGTGATGA	GCATGAACTT	GCTCAGCATT	CAGGTGTTAC	GGCCCACCGT	TATCCTGGCA
13861	AGTCCACTAT	GGCAATACTC	AGCCGGAAAC	CGCTTTTTTC	GCGGTAAAAT	CAGGTATCCC
13921	TGTTGATAAT	GACTGGTTGT	TTCATCTGGT	ATTTGATTAC	GGTGAGCGCT	TATCTTCGCT
13981	GAACTCCGTA	CCCGAATTCA	ATGTGTCAGA	AAACAATGTG	TCTGAAAACA	ATGTGTCTGA
14041	AAAATGGCGT	TGTCGTCCGG	ACAGTTTCTC	CCGCTATGAA	TATGGGTTTG	AAATTCGAAC
14101	CCGTCGCTTG	TGTCGCCAAG	TTCTGATGTT	TCATCAGCTG	AAAGCGCTGG	CAGGGGAAAA
14161	GGTTGCAGAA	GAAACACCGG	CGCTGGTTTC	CCGTCTTATT	CTGGATTATG	ACCTGAACAA
14221	CAAGGTTTCC	TTGCTGCAAA	CGGCCCGCAG	ACTGGCCCAT	GAAACGGACG	GTACGCCAGT
14281	GATGATGTCC	CCGCTGGAAA	TGGATTATCA	ACGTGTTAAT	CATGGCGTGA	ATCTGAACTG
14341	GCAGTCCATG	CCGCAGTTAG	AAAAAATGAA	CACGTTGCAG	CCATACCAAT	TGGTTGATTT
14401	ATATGGAGAA	GGAATTTCCG	GCGTTACTTT	ATCAGGATAC	TCAGAAAGCC	TGGTGGTACC
14461	GTGCTCCGGT	ACGGGATATC	ACTGCCGAAG	GAACGAATGC	GGTTACCTAT	GAGGAGGCGA
14521	AACCACTGCC	ACATATTCCG	GCACAACAGG	AAAGCGCGAT	GTTGTTGGAC	ATCAATGGTG
14581	ACGGGCGTCT	GGATTGGGTG	ATTACGGCAT	CAGGGTTACG	GGGCTACCAC	ACCATGTCAC
14641	CGGAAGGTGA	ATGGACACCC	TTTATTCCAT	TATCCGCTGT	GCCAATGGAA	TATTTCCATC
14701	CGCAGGCAAA	ACTGGCTGAT	ATTGATGGGG	CTGGGCTGCC	TGACTTAGCG	CTTATCGGGC
14761	CAAATAGTGT	ACGTGTCTGG	TCAAATAATC	CGGCAGGATG	GGATCGCGCT	CAGGATGTTA
14821	TTCATTTGTC	AAATAAGCCA	CTGCCGGTTC	CCGGCAAAAA	TAAGCGTCAT	CTTGTCGCAT
14881	TCAGTGATAT	GACAGGCTCC	GGGCAATCAC	ATCTGGTGGA	AGTTACGGCA	AATAGCGTGC
14941	GCTACTGGCC	GAACCTGGGG	CATGGAAAAT	TTGGTGAGCC	TCTGATGATA	ACAGGCTTCC
15001	AAATTACGGG	GAAACGTTTA	ACCCCCACAG	ACTGTATATG	GTAGACCTAA	ATGGCTCAGG

Fig.2.

15061	CACCACCCGA	TTTTATTTAT	GCCCGCAATA	CTTACCTTGA	ACTCTATGCC	AATGAAAGCG
15121	GCAATCATTC	TGCTGAACCT	CAGCGTATTG	ATCTGCCGGA	TGGGGTACGT	TTTGATGATA
15181	CTTGTCGGTT	ACAAATAGCG	GATACACAAG	GATTAGGGAC	TGCCAGCATT	ATTTTGACGA
15241	TCCCCCATAT	GAAGGTGCAG	CACTGGCGAT	TGGATATGAC	CATATTCAAG	CCTTGGCTGC
15301	TGAATGCCGT	CAATAACAAT	ATGGGAACAG	AAACCACGCT	GTATTATCGC	AGCTCTGCCC
15361	AGTTCTGGCT	GGATGAGAAA	TTACAGGCTT	CTGAATCCGG	GATGACGGTG	GTCAGCTACT
15421	TACCGTTCCC	GGTGCATGTG	TTGTGGCGCA	CGGAAGTGCT	GGATGAAATT	TCCGGTAACC
15481	GATTGACCAG	CCATTATCAT	TACTCACATG	GTGCCTGGGA	TGGTCTGGAA	CGGGAGTTTC
15541	GTGGTTTTGG	GCGGGTGACG	CAAACTGATA	TTGATTCACG	GGCGAGTGCG	ACACAGGGGA
15601	CACATGCTGA	ACCACCGGCA	CCTTCGCGCA	CGGTTAATTG	GTACGGCACT	GGCGTACGGG
15661	AAGTCGATAT	TCTTCTGCCC	ACGGAATATT	GGCAGGGGGA	TCAACAGGCA	TTTCCCCATT
15721	TTACCCCACG	CTTTACCCGT	TATGACGAAA	AATCCGGTGG	TGATATGACG	GTCACGCCGA
15781	GCGAACAGGA	AGAATACTGG	TTACATCGAG	CCTTAAAAGG	ACAACGTTTA	CGCAGTGAGC
15841	TGTATGGGGA	TGATGATTCT	ATACTGGCCG	GTACGCCTTA	TTCAGTGGAT	GAATCCCGCA
15901	CCCAAGTACG	TTTGTTACCG	GTGATGGTAT	CGGACGTGCC	TGCGGTACTG	GTTTCGGTGG
15961	CCGAATCCCG	CCAATACCGA	TATGAAGGGG	TTGTTACCGA	TTCCACAGTG	CAGCCAAAAG
16021	ATTGTCCTTA	AATATGATGC	GTTAGGATTT	CCGCAGGACA	ATCTTGAGAT	TGCCTATTCG
16081	AGACGTCCAC	AGCCTGAGTT	CTCGCCTTAT	CCGGATACCC	TGCCCGAAAC	ACTTTTCACC
16141	AGCAGTTTCG	ACGAACAGCA	GATGTTCCTT	CGTCTGACAC	GCCAGCGTTT	TTCTTATCAC
16201	CATCTGAATC	ATGATGATAA	TACGTGGATC	ACAGGGCTTA	TGGATACCTC	ACGCAGTGAC
16261	GCACGTATTT	ATCAAGCCGA	TAAAGTGCCG	GACGGTGGAT	TTTCCCTTGA	ATGGTTTTCT
16321	GCCACAGGTG	CAGGAGCATT	GTTGTTGCCT	GATGCCGCAG	CCGATTATCT	GGGACATCAG
16381	CGTGTAGCAT	ATACCGGTCC	AGAAGAGCAA	CCCGCTATTC	CTCCGCTGGT	GGCATACATT
16441	GAAACCGCAG	AGTTTGATGA	ACGATCGTTG	GCGGCTTTTG	AGGAGGTGAT	GGATGAGCAG
16501	GAGCTGACAA	AACAGCTGAA	TGATGCGGGC	TGGAATACGG	CAAAAGTGCC	GTTCAGTGAA
16561	AAGACAGATT	TCCATGTCTG	GGTGGGACAA	AAGGAATTTA	CAGAATATGC	CGGTGCAGAC
16621	GGATTCTATC	GGCCATTGGT	GCAACGGGAA	ACCAAGCTTA	CAGGTCAAAC	GACAGTGACG
16681	TGGGATAGCC	ATTACTGTGT	TATCACCGCA	ACAGAGGATG	CGGCTGGCCT	GCGTATGCAA
16741	GCGCATTACG	ATTATCGATT	TATGGTTGCG	GATAACACCA	CAGATATCAA	TGATAACTAT
16801	CACACCGTGA	CGTTTGATGC	ACTGGGGACG	GTAACCAGCT	TCCGTTTCTG	GGGGACTGAA
16861	AACGGTGAAA	AACAAGGATA	TACCCCTGCG	GAAAATGAAA	CTGTCCCCTT	TATTGTCCCC
16921	ACAACGGTGG	ATGATGCTCT	GGCATTGAAA	CCCGGCATAC	CTGTTGCAGG	GCTGATGGTT
16981	TATGCCCCTC	TGAGCTGGAT	GGTTCAGGCC	AGCTTTTCTA	ATGATGGGGA	GCTTTATGGA
17041	GAGCTGAAAC	CGGCTGGGAT	CATCACTGAA	GATGGTTATC	TCCTGTCGCT	TGCTTTTCGC
17101	CGCTGGCATC	AAAATAACCC	TGCCGCTGCC	ATGCCAAAGC	AAGTCAATTC	ACAGAACCCA
17161	CCCCATGTAC	TGAGTGTGAT	CACCGACCGC	TATGATGCCG	ATCCGGAACA	ACAATTACGT
17221	CAAACGTTTA	CGTTTAGTGA	TGGTTTTGGG	CGAAACCTTA	CAAACAGCCG	TACGCCATGA
17281	AAGTGGTGAA	GCCTGGGTAC	CTGATGAGTA	TGGAGCCAAT	GTGGCTGAAA	ATCAAGGCGC
17341	CCCTGAAACG	GGCGATTACA	AATTTCCCGT	TGGGCAATTT	CCCGGACGTA	CAGAATATTA
17401	ACGGGAAAAG	GCAAAGCCCC	TGCGTTACGT	TTCAAACCGT	ATTCCTGAAA	TAATTTGGGC
17461	AACTATGTCA	AGTTGACCAA	AAAATGCCCG	GCAGGATATG	TATGCCGATA	CCCATTACTA
17521	TGATCCGTTG	GGGCGTGAAT	ATCAGGTTAT	CACGCCAAAG	GCGGGTTGCG	TCGATCCTTA
17581	TTCACTCCCT	GGTTTGTGGT	GAATGAAGTT	GAAAATGACA	CTCCCGGTGA	ATGACAGCAT
17641	AAAGCTCAGT	GATGCCTGTT	CACTGAACAG	ACATCACTCC	ATTTAGGAAT	GAATCATGAA
17701	GAATTTCGTT	CACAGCAATA	CGCCATCCGT	CACCGTACTG	GACAACCGTG	GTCAGACAGT
17761	ACGCGAAATA	GCCTGGTATC	GGCACCCCGA	TACACCTCAG	GTAACCGATG	AACGCATCAC
17821	CGGTTATCAA	TATGATGCTC	AAGGATCTCT	GACTCAGAGT	ATTGATCCGC	GATTTTATGA
17881	ACGCCAGCAG	ACAGCGAGTG	ACAAGAACGC	CATTACACCC	AATCTTATTC	TCTTGTCATC
17941	ACTCAGTAAG	AAGGCATTGC	GTACGCAAAG	TGTGGATGCC	GGAACCCGTG	TCGCCCTGCA
18001	TGATGTTGCC	GGGCGTCCCG	TTTTAGCTGT	CAGCGCCAAT	GGCGTTAGCC	GAACGTTTCA
18061	GTATGAAAGT	GATAACCTTC	CGGGACGATT	GCTAACGATT	ACCGAGCAGG	TAAAAGGAGA
18121	GAACGCCTGT	ATCACGGAGC	GATTGATTTG	GTCAGGAAAT	ACGCCGGCAG	AAAAAGGCAA
18181	TAATTTGGCC	GGCCAGTGCG	TGGTCCATTA	TGATCCCACC	GGAATGAATC	AAACCAACAG
18241	CATATTGTTA	ACCAGCATAC	CCTTGTCCAT	CACACAGCAA	TTAGTGAAAG	ATGACAGCGA
18301	AGCCGATTGG	CACGGTATGG	ATGAATTTGG	CTGGAAAAAC	GCGCTGGCGC	CGGAAAGCTT
18361	CACTTCTGTC	AGCACAACGG	ATGCTACCGG	CACGGTATTA	ACGAGTACAG	ATGCTGCCGG
18421	AAACAAGCAA	CGTATCGCCT	ATGATGTGGC	CGGTCTGCTT	CAAGGCAGTT	GGTTGGCGCT
18481	GAAGGGGAAA	CAAGAACAAG	TTATCGTGAA	ATCCCTGACC	TATTCGGCTG	CCAGCCAGAA
18541	GCTACGGGAG	GAACATGGTA	ACGGGATAGT	GACTACATAT	ACCTATGAAC	CCGAGACGCA
18601	ACGAGTTATT	GGCATAAAAA	CAGAACGTCC	TTCCGGTCAT	GCCGCTGGGG	AGAAAATTTT
18661	ACAAAACCTG	CGTTATGAAT	ATGATCCTGT	CGGAAATGTG	CTGAAATCAA	CTAATGATGC
18721	TGAAATTACC	CGCTTTTGGC	GCAACCAGAA	AATTGTACCG	GAAAATACTT	ACACCTATGA
18781	CAGCCTGTAC	CAGCTGGTTT	CCGTCACTGG	GCGTGAAATG	GCGAATATTG	GCCGACAAAA
18841	AAACCAGTTA	CCCATCCCCG	CTCTGATTGA	TAACAATACT	TATACGAATT	ACTCTCGCAC

Fig.2.

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18901  TTACGACTAT GATCGTGGGG GAATCTGACC AGAATCGCAT AATTCACGAT CACCGGTAAT
18961  AACTATACAA CGAACATGAC CGTTTCAGAT CACAGCAACC GGGCTGTACT GGAAGAGCTG
19021  GCGCAAGATC CCACTCAGGT GGATATGTTG TTCACCCCCG GCGGGCATCA GACCCGGCTT
19081  GTTCCCGGTC AGGATCTTTT CTGGACACCC CGTGACGAAT TGCAACAAGT GATATTGGTC
19141  AATAGGGAAA ATACGACGCC TGATCAGGAA TTCTACCGTT ATGATGCAGA CAGTCAGCGT
19201  GTCATTAAGA CTCATATTCA GAAGACAGGT AACAGTGAGC AAATACAGCG AACATTATAT
19261  TTGCCAGAGC TGGAATGGCG CACGACATAT AGCGGCAATA CATTAAAAGA GTTTTTGCAG
19321  GTCATCACTG TCGGTGAAGC GGGTCAGGCA CAAGTGCGGG TGCTGCATTG GGAAACAGGC
19381  AAACCGGCGG ATATCAGCAA TGATCAGCTG CGCTACAGTT ATGGCAACCT GATTGGCAGT
19441  AGCGGGCTGG AATTGGGACA GTGACGGGCA GATCATTAGT CAGGAAGAAT ATTACCCCTA
19501  TGGGGGAACC GCCGTGTGGG CACCCGAAAT CAGTCAGAAG CTGATTACAC AAGCCGGCGT
19561  TATTCTGGCA AAGAGCGGGA TGCAACAGGG TTGTATTACT ACGGCTATCG TTATTATCAA
19621  TCGTGGACAG GGCGATGGTT GAGTGTAGAT CCTGCCGGTG AGGCCGATGG TCTCAATTTG
19681  TTCCGAATGT GCAGGAATAA CCCCATCGTT TTTTCTGATT CTGATGGTCG TTTCCCCGGT
19741  CAGGGTGTCC TTGCCTGGAT AGGGAAAAAA GCGTATCGAA AGGCAGTCAA CATCACGACA
19801  GAACACCTGC TTGAACAAGG CGCTTCCTTT GATACGTTCT TGAAATTAAA CCGAGGATTG
19861  CGAACGTTTG TTTTGGGTGT GGGGGTACAA GTCTGGGGGT GAAGCGGCCA CGATTGCAGG
19921  AGCGTCGCCT TGGGGGATCG TCGGGGCTGC CATTGGTGGT TTTGTCTCCG GGGCGGTGAT
19981  GGGGTTTTTC GCGAACAACA TCTCAGAAAA AATTGGGGAA GTTTTAAGTT ATCTGACGCG
20041  TAAACGTTCT GCTCCTGTTC AGGTAGGCGC TTTTGTTGTC ACATCGCTTG TGACGTCTGC
20101  ACTATTTAAC AGCTCTTCGA CAGGTACCGC CATTTCCGCA GCAACAGCGG TCACCGTTGG
20161  AGGATTAATG GCTTTAGCCG GAGAACATAA CACGGGCATG GCTATCAGTA TTGCCACACC
20221  CGCCGGACAA AGTACGCTGG ATACGCTCAG GCCCGGTAAT GTCAGCGCGC CAGAGCGGTT
20281  AGGGCACTAT CAGGCGCAAT TATTGGCGGC ATATTACTTG GCCGCCATCA GGGAAGTTCT
20341  GAGCTGGGTG AACGGGCAGC GATTGGTGCT ATGTATGGTG CTCGATGGGG AAGGATCATT
20401  GGTAATCTAT GGGATGGCCC TTATCGGTTT ATCGGCAGGT TACTGCTCAG AAGAGGCATT
20461  AGCTCTGCCA TTTCCCACGC TGTCAGTTCC AGGAGCTGGT TTGGCCGAAT GATAGGAGAA
20521  AGTGTCGGGA GAAATATTTC TGAAGTATTA TTACCTTATA GCCGTACACC CGGTGAATGG
20581  GTTGGTGCAG CCATTGGCGG GACAGCCGCG GCCGCTCATC ATGCCGTTGG AGGGGAAGTT
20641  GCCAATGCCG CTAGCCGGGT TACCTGGAGC GGCTTTAAGC GGGCTTTTAA TAACTTCTTC
20701  TTTAACGCCT CTGCACGTCA TAATGAATCC GAAGCATAAC AATCATGTTC ATTCCCACTT
20761  TGTCATGGAT GACAAGGTGG GTTTTTCGGA TGTGTGGACA GAGACCCGTA CAGGGTCTCT
20821  GTCCAGTTAA TTTTTGGATC AAGAACGAAT GGTGTAACGG ATATGCAAAA TGATATCGCT
20881  CAGGCTGAGC AATAAGCTTT TCTGTTTACC ACTGATACCG GGAAAACTGA GGGTTAATGT
20941  GCCTGTATCG GCCACAGGAA GCCCTTCAAA TGGCAGGTAC TTAGCATCAT TGAAATCCAT
21001  CTGGAATTGA CCACTGTCAT TCATGCCATG TGAGATCACA ATCGCTTTGC AGCCACGTGG
21061  CATCATTGTA CTGCCGCCAT AACTCAGTAT TGCCCGGACA TCCTGATAAG GCCCTAAAAG
21121  GGCAGGTAAC GTCACACTGA TTTGTTTGAT ACGGCGTGTA TTACCTAAAC CGTCAGGATA
21181  ATCGGTAGCA ATATTCAGAT CCGATAATTT GAGGCTGGCT TGCAGTTGTG TCCCTTCGAC
21241  GTTCAAACCG TTAAGCGTTG TGCCTGCACT GCCTTCACCT GCATTGACTA ACTCAGTCAC
21301  TTTATCTTTT AAAATGAAAC TATTTTCTGT CAGACCAGCA TACACTTCAG CCAGAGAAAC
21361  GGTTCTGGTG ACCTCCAGTG CCCGTTCATC TTTTTCCAAA TAGCTTTTTT CCATCTGTGC
21421  TAAATTCAGC ATCAGGGTTT CACCCGCTAA TAAACCCGCA TAAGTCCCAT GCCAAGCACC
21481  TGGTTTAATA AAGTGTGCTG CCGCATTATT CAATTCATAC TGATAAGTTT GCTCTGCCAT
21541  TAAACAGAGT GAGACCGCCA AATCATAAAA CTGATAATAA ATAGCGGACA ACGTTCCACG
21601  GAGCCAGTTG TATAGCGCTG CATTACTGAA TTTACTTTGC AGAAAGGCTA ACTGCGCCTG
21661  AGTTTGTGCC TGCTGAGTTT CCAGATAGTT TTTTTGTAAT ACTGCCGCTT CACGACGTAC
21721  AGCCAGCGTC GCTAATTGAG CATCAATTTG TTTTATCTCA GCTTCCGCAT TATTGCGCTG
21781  AATTTCCCAC TCTTGCCGAC GGCGACGGTA TATTTCTGAT TGGCTGATTT TGTCTGCGGC
21841  AATACGTGTT GCTGACGCAG AAATTTCGAT ACCAATCGCA CTGGCATTGA AAAGCGCCCC
21901  AAAACGGGAA CCTCCCACAG CAAAACCGTA AATATTGGGG ACGAGATCTG CCGCGGCGGC
21961  GGCCATATGC AGGGCTGTGC CGCTGGTGCT CAAGACCGAT GAAGAGAGGT AAAGATCCAT
22021  CGCTTGTTTT TCACCAGCGT TAACATCTTC GTCGTACAGC GTATTGAAAC TGTCAAAACG
22081  AGACTGTGCA CCATGACGGC TTTCTTGAAG CGCCAATTTA TCAGCATCAA TTTCAGCCAT
22141  GACCTTATCC TGCATTTTAA TACTTTGCAG GGCTAACTCA CTGCCTTGAG TTTGCAGTAT
22201  TTCAGCCAAG GCTTCTGCAT CCTGCCGTTC AGTAATGCTG AGCAGGGTAT TGCCAAATTG
22261  TATCAACTGG CTTACCCCCC ACTTGGCATT TTCCAGAATC ACCGGAAAAC GGTACATCGG
22321  CATCACTGCA TGAGGTAAAT CGCCGCCGCC TTGTGAAGCA GTGATGGCAG CACTGAGTAA
22381  CATGGACGGA TCTGCGGGCG TGGCATAGAG AGATAATGAC AGTGGCTGAC CGTCGATTGT
22441  CAGGTTATGG CGTAAGTTAT AGAGGCGTTG CGTCAATGTC TGCCAGTAAC CTTGCAGTTT
22501  TTTATTAATT TGAGGGAGGA ACAATGCGGT TAACGAAATT TGCCGTACGT TTCGTGGGTA
22561  ATGCAGCGCG CTGACGCAGT TGCAGCATTT TATGTTGATA ATGATGCCGC ATTGTTTGGC
22621  TGGCAGCTTC TTCCAGCCGT GGCTCTGACC AATCGTTATC CAATGAAAAA TAAGGCTCAT
22681  CACCCAATAA AGTGAGCGCC TGTACATACC ACATTTTAGC TTCGTTTAAG GTATCACGTT
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09/242843

Fig.2.

22741	CAAGCTGGCG	ATAGGCGCTA	TCTCCGCGGG	TAATCAACAA	ATCCAGCATT	TTCATAAAGG
22801	TAGCCACTTT	ATAGTGCATC	GGATCATGCT	GGGCAACGGC	GTCCGGATCG	ACCGAATCCA
22861	GCGGATTGGC	ATTCCAGGAC	GTATCTTCCT	CCAATGGGCG	GACGTTCCAG	TAATAATCCT
22921	GCATTTCACC	CTGAACCGAA	TATCCGGTCG	GGTTCAGATA	TAGCGCAGCC	AGCGTGTCGA
22981	TCCGGTAAAA	TCTGCTCTTG	CAATAAGCGC	TGGAATACCA	TCATGGGCGT	TGTAATAGAA
23041	CAATCCCAAG	AAATAGATTG	CATTGGCGCC	GTTTGAAATC	CATGGGTTCA	GTGTTATTTT
23101	TCATGACACG	ACTTGAATAC	CCCTTTTATA	TTTTTTGATA	TTTTTTACTA	TCCCCTGTTG
23161	TGTCATTCCC	GAATCATGAT	CGGCATCATT	AGTGAATATA	AATTGATTTT	TCGTCTCATC
23221	AAAATAAAAG	AAAGCAGATT	CCCAGGATTT	GTCATAGATA	ATTTTTTTGT	ACCCAACCCC
23281	TAATCTGACA	CCTTCACGTA	TGTAATATCC	TTTAGCATAG	GGAACAAAGA	GCGTTACTGT
23341	GGTTTCAATA	TCAGATAACA	TTCCTTCGTA	ATAAGGTTGT	CTGGCAGAAT	TGCCATCAAT
23401	ATTCCCAATA	TGGATCTTAA	ACCAACGTTC	ATCACCATGC	TCCTCTTTAT	TGTAGGGGGG
23461	CAACTTAAAT	GTCGCATAAA	ACCCTTCACC	TAATTGCGGC	TCTGGTAAAT	TTTGCGTTTC
23521	CATACTTAAA	ACATTATCAA	TACCAATATT	GGCTCTTTCA	GCTAATTTTC	TGGAAAATAA
23581	AGTATTTAAC	CGGGTTCTGT	AAGGGCCAAT	CTGCATATAT	TGTGTGCCTG	ATGGCATTTT
23641	ATGCAGTGAT	ATAACGTTAC	TTGTATCTTT	GGATTTTAGT	TTTATATGAA	TTGGCGATTC
23701	AATAACAATA	TCGTTATAAC	CGCCGTCGGG	TTGCTTAATA	ATAAACTCGC	TCACCAGAGG
23761	AATATCATAG	CCTTCAATAT	CAACTTTTAC	TTGATTAAAA	TCATATACCA	TAGGGTCAGA
23821	TTCGTGTGAA	GGTTTAGATG	CCACATGGTC	TTCAGCATTT	AACTCCACTA	GAATATCAGA
23881	GCCATTTTTT	AATAAAAAAC	TAATGTTTTT	ATCTTGGATC	TGTTCGATCA	TAGATGAAGC
23941	AAGTTTTATT	ATCTGTGGCT	GGTTGAACAT	AAATACACCC	ATGGATCCTC	GCGAAGGAAC
24001	AGTGCCGCAA	TATTTCCCAT	GTTATTAATG	ATTGAAACAT	CATTAGTAAA	TGATTCACAT
24061	ATAGTATGCC	ATACTCCTGT	GTTATCTTTC	CAATCTAATA	CTATGTTAGT	ATCAAGTTTG
24121	AATTCAGCAT	CATCTGATTC	ATAATCATAA	TTTATACCAA	CTCCAATTTC	TGATTTTCTA
24181	GGAATTTTTT	CCTTGGTTCT	TAGATGCATT	AACACTCTAA	AATATTCGGC	ATTTTTAAGA
24241	TCGATGGAAA	TAATAAAATC	CAAAGTTCCA	TAATGAAAAA	CTTCTTCTTC	TTTTCCAAGC
24301	ATTTCATCAT	GTCTATCATA	ATCAAATAAA	ATAACCGTTT	CATCTTCTAC	CATCGATAAC
24361	AGGTATTTAA	CCTCATCATT	ATATATATTG	CCTTTTGAAA	AATTAATTTC	CATTGAAGGA
24421	TTGAACGTTA	AATTAATATG	ACCATTTCCT	GGTGATATAT	ACGAGAGATC	AAAAATATTT
24481	CCGGTAAAAC	TGGCTAATTT	ATTTTTTGTG	GTTATAGATT	CCTTATATTC	GGCCAAATAA
24541	TCTGTAGCAA	ATTGATTGTT	GACTTTGTAT	TCTGTCCTGG	TATCAAGTTC	TGATAATGTG
24601	CTCTTAACAA	TGGCGTCTAA	ATCATTTTCT	GTGAGAATGG	ATAATGTCAT	ATCAGGGTTA
24661	ATGGTCATCC	CTTCTCTTGC	AGGAAGACTA	TTAAAAGAAT	AATTGTCTTT	TTTCTCATGG
24721	AAATAAACAA	TAATGACGTC	TTTTTCATAA	TCAGAAGAAC	AATACATACC	AATGCTGGCT
24781	TTTTTATTGA	TCAGGTTTTC	TATTTTATCA	GTCACATTAA	AATTAAACGG	TGAGCTCCAG
24841	CTGCCATCAT	AACGAATATG	TGACAGTTTT	AATATATAAT	CAGTGATATC	TATCTTGCCA
24901	TCTTCACTTT	CATTTTTCAG	CTCTTTTTGT	TCCAGCCACA	GTAAATACAA	ACGAGACTTG
24961	TAAATAACAG	GTCTGATATT	TTCCTGCCAT	ACATTGATGG	GTATTTCAAT	TTTTTTCCAT
25021	TCTCCCCAGG	CATTGGCAGC	AAATTGACCG	TGCTGGCACT	TTTGGTGATC	GACATTGCGC
25081	CAATAATATA	TTCTGGGTTC	TGTCTGGCTA	TAACCAATTA	AATAAGTGAG	CCCCTCATTG
25141	ACATTAATAC	TGTCATGATA	TCCGCTAATC	ACCTGCAAGT	TAGCGACATC	TTCAAATGCG
25201	GTCAGATAAT	TTTTAAAGCT	ATCTTCAACG	GTATCGATAT	TTAACTGACT	TTGGGAAAGT
25261	TGCTGTAACA	GGTTGTTCAT	CATACCTGTC	TGACCAATAC	GAATCGTGGG	GTCGATATAG
25321	TTTTCCGGAT	AATAGGCCAG	TTCAGATACG	CCGGCCCAGG	TGCTATACCG	TCGATTGTAG
25381	GTTTCCCAGT	CGCAGAAGAA	CTGACGGGTT	TTCACTGGCT	TTGATACTTT	TCCTTCAACA
25441	TTATTCAACG	CCCGGTTGAC	ATATAACTGA	ATGCTGGCAA	TGGCTTCTGC	CACACGGGTG
25501	GTTTTCACTT	GGGCAGAAAC	TTGGTTATCA	ATCAGCAGAT	AGCTGTACAA	CTCATCCCGG
25561	CTCTTAATCT	GTTGAGGTGC	ACCATTTTTG	ATGTAGTAAG	CACTGGCCGC	TGTCGTCGTG
25621	GCTTCATCCA	GCCATGCCTG	AAGCTGGTCG	GATTGTTGAC	TGTTCAGTCC	CGCCTGCAAC
25681	AAAGTACTGG	CGGCTTGCCA	ATCATCAAAT	GTTGGCATCG	GGGTTTCCGG	TTCACCGACA
25741	TATTTTAATT	TTATGAGTGC	AGCAACACCA	TCCGGGGTAA	TACCCAATGT	AGCAGCGACA
25801	TCCAGCCATT	GCAGAGTGAC	ATCTATAAGT	TCTCCAGTTG	GTAAAGGTAT	TCACTCCCAA
25861	ACCGGTCTGT	TGCAATGCTT	GTGTCACAAC	CTGAGCATCA	AAATTTTAAC	GCCACCGCCA
25921	AATTGTTCGG	CAGTCAACGC	TCCTAAGTTC	CAAATGCTGT	TAAGATTCTG	TCGCGTAGCT
25981	TCACAACGCA	TGATCACAGC	ATGGAAGCGG	GTCAGCGCTT	GCAAAGTGGG	GAGATCATGT
26041	TGCAGTGCTG	TGGTTTCTGA	TTGGAATTTC	TCCGGTTTTG	TCACCAACAG	GGTCAGTTCG
26101	TTTTCGCTGA	GTCCAATATT	GCGCACAATC	AGAGAAAGTT	GCCCCAGTAC	CTGACAAAAA
26161	GCCACCATGT	TGCTGGTTTC	ATTCTCTGAG	CGATCACGGT	TAGCCGCAAT	AATCATGAAA
26221	TCATCGAATG	TCAGTCCTTG	TGGTTTTATC	TGATTAATCC	ACAGCAAAAT	AGTTTCTGCT
26281	GTTTTGGCTG	AATCCATTTG	AATGCTGGCA	GCAATCAGCG	GGGCAGCTGC	ACGGATCAGT
26341	TCGTCATCAC	CGAGTGAAAG	TGTTGATAAT	CCATTACTTA	GTGTCGTGAT	AAGGTTTTCA
26401	ATATCCGGCG	TAAGGACAGT	GCTGTAATTA	TCCGTGGTCA	TCAGAAACAC	ATCACTGACA
26461	GACCATTTCT	GTGTTGTCAG	CCACTGGGTG	CATTGGAACA	GAAAGCTGAT	TAATTGCGTT
26521	AATGCTGTAT	CAGAAAAAAG	GGCAATTTTC	GTGTTCACAT	AGGGAGAAAC	CGACAACAAC

Fig.2.

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26581  ATGGATAATT CATTCACTGT CAGATGATGA ATGTCTGCCA GCAGACGAAC GCGATAAAGC
26641  AGAGACAGGT TCTCGATGGA ACACATAAAT TCTGGATTTG TTCCGCCATT AGCCAGTTTC
26701  CATAATGTAT ACAGTTCAGT ATCATTCACT CTGAAAGCAC GTTTCATTAT TCCCAAATAA
26761  AAATGGTTTT TTGATTCACC GGGGGTTAAA TCCAGTTTGG TATTATCAGC AGAAAACTCT
26821  TGGCCATTTA ATAGCGGTGT ATTGAACAGC ATTGTAAAAT GACTGGGTTG TTGTTTAGTG
26881  GAATATTGGC TGATATCTGA ATGACACAAT ACCAGCGCAT CGCTGACGCT AATATTATAG
26941  TGCTGCATAT AATATTGAAC ATAAAACAGC TTACCCAACA CATTGCTGTC AATGGTTAAG
27001  TCATCATAAA TACTTTCTAT TACTTGCCAG ATATCTTCTG GAGATATGCC TGTGGCTTTA
27061  TACAAACGAA TCGCTTTATT CAGCTTTAAC AGGAATATAT CACCGGGAAC TCCATCATTT
27121  TAAAGTGTGC ATTGGCATTG ATAGCATCCG ACGGATTTGG TTAACTCGCC ATAAGCGGAG
27181  TGTTATACCG TTGGTGATTT GCTCTGTCGT CAATTTAATG GGAATACTGT AATGGGTATT
27241  AGCAATGGGG ACGAAATTTT TATCTTGGTA TATATATTCT TTATCTCCAT TCTGGAGACG
27301  AAAATCCAAG TGGTCAGGTT CTGTTTTTTT TACACTGAAA TTATATTTGT ATTCATTTTC
27361  TTTGATTGGA ATTAGCTCTG CATAGTTTAA ATGTGAATCG TAGAAATCTT TGCGGGTTCG
27421  CTTAATCAAT CTTGCCGTTG CCGTATCATT CCCGTCATTG ACCAATGTTA TCAGTTGCTC
27481  ATTCTTATAC TGTTGATTTG TATTTTTCTT ACCGAAGGAG AGATTGACAA ATAAACTGAG
27541  TTCATCATAA GACAAATCGT AGTAGCGAGC CAAAGAAGCA TAACTCTTAA AAATCAGTAC
27601  ATCATCTGTA CCGAAATTTT TCTTCATCAG TTCTGTTGAA TTTTCCGGTG TAATTTCTTC
27661  TACAAGGATT TGATACAATT CAGGCGATAT ATCAGTCTTA ATAGCCAGTA GCGATGTTGG
27721  GTCCATTAAT TCCGCTACGT CTGTATTACG GCTAAATGCG GTGAGGTTTT TATCTTGCAA
27781  TAAAATTGCC TGACGGGCTG ACTCATACGG CAGATGATAG GGTGTCATGC CGGTTTGCCG
27841  GTAAGTGGAC AACATTTTCA TTACACCGTT ATAGTCAGTT TTCTCTAACG TCTGAATATT
27901  ATGCAGCAGT AATTCATTAG ATAAGGATAA TGTGGAAATT TCTTCATCCA TATTATTCTG
27961  TGTCAGTGCC AGTGAAGCAA TGTCGGGGCG TCGTTTATTC AGGTGATATT GAGAATTGTC
28021  AGGATGAAAA TCTTTCGCTT CCCGATATAA TTCTGTTAAA TAAGCCGCTG GTGAAAATAT
28081  GGAAGCAATT GATCCCGGTT TTACAAAACG GTGGGCGCGG CCATAAAACC AACTGTTGTA
28141  ACTATTGTTT AGGGTTGACG GTGTAATATT AAGGTTAGTG ATATTAGCCA GTTGTGGATT
28201  AGCACGGGAC AAAATGCGCA GTTCTTCAAG TTTATTCTGT TTTGATTCCT GATGAGCCTG
28261  TTGATATAAA AAGTCTGTTT CTCGCCACGT CAGAGTTCCA CTTGTCCTAT GACGAAATTC
28321  GCTGAAAGAC ATAAACGAAA TGTTTGTCAA TAATAAAGTA TCACCAGCCT TTTTCTATTT
28381  ATCTTATCTA ACAGTTCATT AACTTTTATC ATATAAATCC TTAAGTTATT GTCAATTTAA
28441  TGATTAATGG TTTTTAGGTG GAGATTATTA TAATCTGATA GGAATATTAT GGTTAATTAA
28501  ATTGATACTG ATTTATCGCT CTATTCTTTC AATAAAAAAT AAAGAACTTC CCTATAATAC
28561  ATGGATTTAA ATAATGAATA CCGTATGTTA AAAATTAAAT TTTAACAAAC TTTCATGAAA
28621  AAATTCAACT CAACAATTGT TTAAATATTT TTAATTGTGT TTGTGCTGTT TGAAAAATGA
28681  ATGACTAATA TTTATCTATG AAAGATTATT TATTGAGGAT GTCTTGCTTG GTTTCAGGGG
28741  GCTACGTTGG AGTCAGATAA ATGTGTGCAA AAAGAAATCC TTAATAAAGT TGCGTAATTA
28801  CAAAAGTTGG TATATCGTGA CAAGAGTGAT AGTAATGTCA CATAATTTAT TGAATACCCG
28861  AACCTCGCAA ATGCGGGGTT TTTCTTCGCA TAATCAAAGA GAAAGCTATG AAAAAAACAC
28921  TGATTACTCT TATTCTCAGT ACCCTTTCTT TTGGTGCTTT GGCACAGCAG GGTGGCTTCG
28981  TTTCCCCGGA CAGCACAGAC TATACTCAGG GTGGATTTAA AGGTCCAACT CCCAACCTGA
29041  CCAGCGTTGC TCAAGCAAAA TCTTTTCGTG ATGATGCGTG GGTTGTTCTG GAAGGAAACA
29101  TTGTTAAACA GGTTGGTCAC GAACTCTATG AATTCGCGGC CGCATAATAC GACTCACTAT
29161  AGGGATCGCT TATTACGGAC TTATCCGGAA AGCTATCTGG AACCCCTGTT ACGCCTGAAT
29221  AAAACAGAAT TCAGGGATAA CAGTGGTTCT GTTTATGTTG ACATTGATGA TAAGCGCTGG
29281  ATGGGTCTGA CGGCCACTCC AACTGACAAA GTTCGTATCG AAGGTGAAGT GGACAAAGAC
29341  TGGAACAGTG TTGAAATTGA TGTCAAAACT ATCCGCATAG TGAAATAACT CAAGCACTTT
29401  GAATATAGCC CCGCACTCGC GGGGTTTTTT GCTTTCTGGG AGTCGGAAGT TTAACCGTAG
29461  TGACGAGGAT CAAAACTAAG TTAACGGCAG TGGTCACTGA TTTGGTGCAT AAGTTATCAA
29521  AAGTTAAAAA TCAAAACTTA TTTTTTATTT AATAGAGGAA TGTCACCCTG TAGGTGAATA
29581  ACGTTGACGG ATGTAAATAT ACAGTATTAT AGTCCTTTGA TATGTTATTA AATTGAAAAA
29641  CCTTTAAACT ATATTCGGGG GAAATTATTA TGTCAGATGT TCGTAATATT ATTAATGTTG
29701  ATAACAATTT TGGTTGTGAA TATAAAGCGG ATTTATTTAA ATAAGTTTTC ATAATTGTGA
29761  TACACCCATT TTTCTCATCC CCGGTTTTTG CTGTTGTAAG GAAGCGGTTT CCATGAAGAT
29821  TTTGACATGG TTAAGCAACT GCCACATAAA TTGGCAGCAG TGGTTTCGTG TCACGGTTTC
29881  ATGCAAGGAT TGCCATAGAC GTTCAATTTT ATTCAACCAC GGGCAATAGG TCGGTAAAAA
29941  GAGAAGATTA AATTTGGGAT TCTTTGCCAG CCAAACCCTG ACCTTCCGGC TCTTATGAAT
30001  GCAATAGTTA TCTAAAATTA ACGTGATGGT TTTGGCATTA ACATATTGAT TGTTAATTTC
30061  ATCTAACAAT TTGATAAATA AATCTGAGTT CTTTCTCAAG CTACCGACAT AAGTGATTTC
30121  TTTCGTTTTC GCGTTGAGGC AATTGGCAAG GTAGTGTTTT TGGTTCTTTC CGGGGGTAAC
30181  AACACGCTTT TGTTGCCCTT TGAAGCACCA GTCTGCACCG ATTTTCGGGT TCAGGTTGAT
30241  GTCCACCTCA TCCTCATAGA AGACCGGGTG TTTCTCTTGA GGCATTGGAT AACGTCTCGC
30301  TGATTTTTGC CATTTTTTCA TCATACTCAG GGTCAGGCAA TTTTACGGTT GGTGCCGCCC
30361  TTCGCCAAAC GATGCCCGTC CGGCAAAAGT AGCGATAGAG GGTACTTTGA GAGAGCGATG
```

Fig.2.

30421	TATTCAGTAG	CTCATTGATT	TTAAGTGTAA	TAAGCTCAAG	GCTCCATCGT	GAACGGAGAT
30481	AGCCAAAATG	TTGTGGCGAG	TGCTGTAATA	AGAAAGAAAT	GACTGTGAAG	AGCGGAGCTA
30541	AGTTCCAGAT	GGCAGGCCTT	CCCGCCGGGA	GGCTTTTAAG	TCCTTCCAAC	CCGTATAATG
30601	TTAACCAATT	TACCCAACGA	TGAACGGAAG	AACGTGAACA	GTGAAGCGTT	CTGGAAACGT
30661	GAGAAACCGT	ACTCCCTTCA	TGTAACATCA	AGAGCGCGGT	GAAGCGACGT	GCATAGTCCT
30721	TATCCCGGGT	TTTCTGGATA	GCTTTTTTCA	TCGGACGTCG	TTCATTTCGG	GGTATTGATG
30781	TTATGATTGG	CATGACTCAG	TCCATTTTGG	GATTTGTTTT	GATTTGGCGA	TTAATCAGAT
30841	CGCGAAAATC	GGACTGAGTT	CCCTTCAAGT	GATCTACTAT	TTTGAAATCT	TATTTAATCA
30901	GGAGTCAGCA	AATGAGTTAT	TCCCCATAAT	ACCTGACCAT	GTGGTTGTTT	ATCCGGGAAA
30961	TGATTCATCT	ACCGGTGGTA	TGTGGATTCC	TTGGTGCGAT	AGTCAGAAAG	ATATTGACTC
31021	TGGCCATTAT	ATCAAAGTTA	CTTTCAGTAA	AAAGGACGCT	GCTGATATTG	TGAACTACAT
31081	GTTTCAACAT	GGCAGTTATG	TTTATTTTAC	AGACAGTAGT	AAACAATTTA	GCAATAAGCA
31141	AATTATGTCT	GGTGATTCAG	CTAAAGGCAA	AGGGGATTAT	AAGCTTGAAA	TTAAAACAAA
31201	CGGGAACCTT	CCACTGATGG	TATTGAATAA	ATATTGATTC	ATTATTATTT	ATGGATAAGA
31261	AATTAAGTTT	ATATTTCATC	TGGTTTCTGC	AATTAAGTTT	TAAAAATTAA	TTCTACTTTT
31321	TTTATGGTTT	TATATTTAAT	GCCAATCATA	TTATTTTTCT	TATAATAATT	GATAGTTTAT
31381	TTATATAGTA	AATAAATTCT	GTTGGATGTG	ATTATTATTG	TGAGACGGTA	ATAATTAACA
31441	TAACAGAAAA	TTCATGGTTA	GGAAATTCAA	TCAACTTTTG	TCCGGTTTCC	TGACCATGAA
31501	GAGCTGTATT	TACTGTAGAA	CTCGCATTGA	TACTGGATTG	ATTAGCCGGA	CGAGTGTTGG
31561	GTCAGCAGAT	AATATGTTGT	ATATTGGCTG	TGGATTTTTC	AGCGAGATGA	TAGCTTTGGC
31621	AGTAAAGGCG	ATTAATAACC	GATAAAACAG	AGAGACGGAT	TGTGGCCAGG	AAAGCAAAAA
31681	AGCCTCACCA	TGACGCGTTA	TTCAAACATT	TTTTAACCCA	ACCAGAAACC	GCCCGGGAAT
31741	TTTTATCCCT	TTATCTGCCG	GAAGCGATCC	GGTCAGTGTG	TGATTTACCA	CACTAAAACT
31801	GGAACCGGCA	GCTTTGTGGA	CAGGCAATTA	CGTCAGTTGC	ACAGTGATGT	GCTGTATTCT
31861	GTCGAGACAA	CCCACGGGGA	CGGTTACATT	TATTGCCTGA	TTGAACACCA	GTCCACGCCT
31921	GATCCGTTAA	TGGCCTGGCG	GCTGATGTAT	TATTCGCTGT	CAGCCATGGC	TGCGCATCTG
31981	AAAAAAGGAC	ATACTGAACT	CCCTTTGGTC	GTCCCCCTGC	TGTTTTATCA	TGGTGAGGTG
32041	AGGCCTTACC	CTTACTCAAA	TCGATGGCTG	GATTGTTTTA	CACTCTCTGA	ACACGCGGCT
32101	CACCTGTATA	ATCAGCCCCT	GCCGTTGGTG	GATATCAGTG	CGCTCAGTGA	TGAAGAGATC
32161	CTGACACATA	AAAGCATTGC	CTTGATGGAG	CTGGTACAAA	AACATATCCG	TTGCCGGGAT
32221	ATGCTGGAGT	GGGTTCCCCA	ATTGGTGGCG	TTGTTGAATG	CCGGTTATAA	TAGCGCCGAA
32281	CAGCGCCATG	TTGTGTTAAG	CTATATTTTA	CTGAATGGAC	ATACGCTGGA	TCTCGCCCAG
32341	TTTGTCCATC	AACTGACTGA	ACAATCTCCG	GAGCATGAAA	CCATGTTGAT	GACTATTGCA
32401	GAACAGCTTG	AACAAAAAGG	GCGTGAGCAA	GGCCGGACAG	AAGGCAGAAC	AGAAGGCAGA
32461	GCTGAAGGAC	GGGAAGAAGG	CAAGCTGGAA	ACGGCGCGCG	CATTATTACG	GCATGGTGTC
32521	AGTCTGGACA	TCATTGTCAC	CAGTACCGGC	CTGAGCCGGG	AGAAAATTGA	AGCGTTAAAG
32581	CATTAAATGG	ATACGCTTTT	TCACAGCAGG	ATATGGTGAC	CCCTGTGAGG	CCACCGGAAA
32641	ATTTTATTTA	CTACGATTTA	CGACGGGTTA	CTTTAGGAAG	CTGAATGAGA	CGTCCTTTGT
32701	TATATAACGG	TCCCATATCA	ATCTTCTCTT	TTCCGCGTAC	AGGTAAGTAA	CCCAAACCTT
32761	CGTGAGCAGC	ATTTGCCAAC	AGGCCATCAT	CCTGATCGCC	TGACCAAGAG	AAGATCCCGC
32821	CCAATTTCAT	TTTGGTTGCA	TAAATTCCCT	TATGCAGCAC	AGTGCGGGGC	GTATCCAGTG
32881	AAATCCAGTG	ACCACCGTCA	GCATTAAAGA	GTGCGTCAGC	GTCGGTTTCC	GTGTCTGTCA
32941	CCAGTTCAAA	CTGATTTTTC	CCGCGTGCAA	TTTCATATTC	CGCATCGTAT	TGGTTATTCA
33001	GCAGACAGAA	GAATTCCGGA	GCACCTTTTT	CCATCGTGCC	CAGTGGCTCT	CCTGTTCTGT
33061	TATAGCGGCG	CGTTGTCAGA	TCAGCACCCA	GACATGAACG	TCCATAGTTA	GCAAATCCGA
33121	GGTGAATTTT	CTCCGGTTGT	ACACCTTGTG	ACAGTAAAAA	GCGGATCGCC	TCATCTGCCG
33181	AGTAATCCAT	GTCCCGATCA	GGATTGGGCG	GAGGAGGGTT	ATCGCCGTCA	TATTCATATC
33241	TGGGGGGATA	CAGGTTAGTA	TGGTGACCGA	TGTATTCTGC	CCAACCGGTA	CCAAAGAAGT
33301	CGTAGGTCAT	CACAAAGATA	TTGTCTAAAT	AAGGTGCGAT	TTCTTTGAAG	CTGGACTTCT
33361	CCATTTTGGC	AACGACGGCG	CTACAGGCTA	TCGTGATTTC	TTTACGGGCC	CGGGTTCCAA
33421	AGGCGATGTT	CAGTGCTTCA	CGCAGCTCTT	TCACTAACAA	AACATAGTTT	GGGCCATCAT
33481	GTTCCGGGTC	GAATTCATTA	CCTTCTTCAC	CTGTGGCGCC	GGGGTATTCC	CAGTCGATAT
33541	CCACCGCAGT	AAACATGGGA	AAACGCCGGG	AAGAAGTCGA	CGATGCTACT	CACAAATGTA
33601	GCACGTTGCT	CAGGATCTTT	GGCCATCACA	GAGAAATACC	CTGACATACT	CCAGCCGCCG
33661	ATACTGAATG	CGAGTTCCAG	CTTATGCCCT	GCCTGTTTTG	CTCGCGCTTT	CAGATTACGC
33721	AATCCCCCCA	GTAAACCGGA	GGCTGCATCC	TGATTGTAAT	ATTGCAAGAA	ATTCTTCGGG
33781	CTGGCATCAC	GGCGCTGATC	CGCGTCCAGA	CCGACATTGC	GTGTGGTGCC	TAAATCACCA
33841	TAAGGATCAA	CGGGTACAAT	ATGGCCTAAT	GTAATAGGGG	CAATCTGGCC	ACTGCTGGCT
33901	TCTGCTTGCC	GGTTCCACCC	GTCAACAACC	TCATTAATCC	GTTCGGATAA	CTTGCCTTTG
33961	TCACCGTTGA	CGGCCATAAA	ACTGAAAATC	AGGCGGTCGT	AGGCGGTAGG	CGGGATTTTT
34021	TCCAGATCAA	AACCACGGCC	GGGGGCATCG	TCGCTGGTCA	GCGCAGTGTT	ATCCTGGGTT
34081	TCTGGCGACA	AACGCGCATC	ATACTGGCAC	CAGTCAGTAA	TATAGGCAGA	GACTTTAGGC
34141	AGCGGTTCTG	TATTTTCCGG	ATCAACTTCA	TATTCGTTGT	ACAGGGACTT	GGCAACACGT
34201	GCTGAAGAAT	AACTCAAAGG	AGTTCCGCTG	CCGTCAGGTT	TATATCCCAC	CTTCTGATAG

Fig.2.

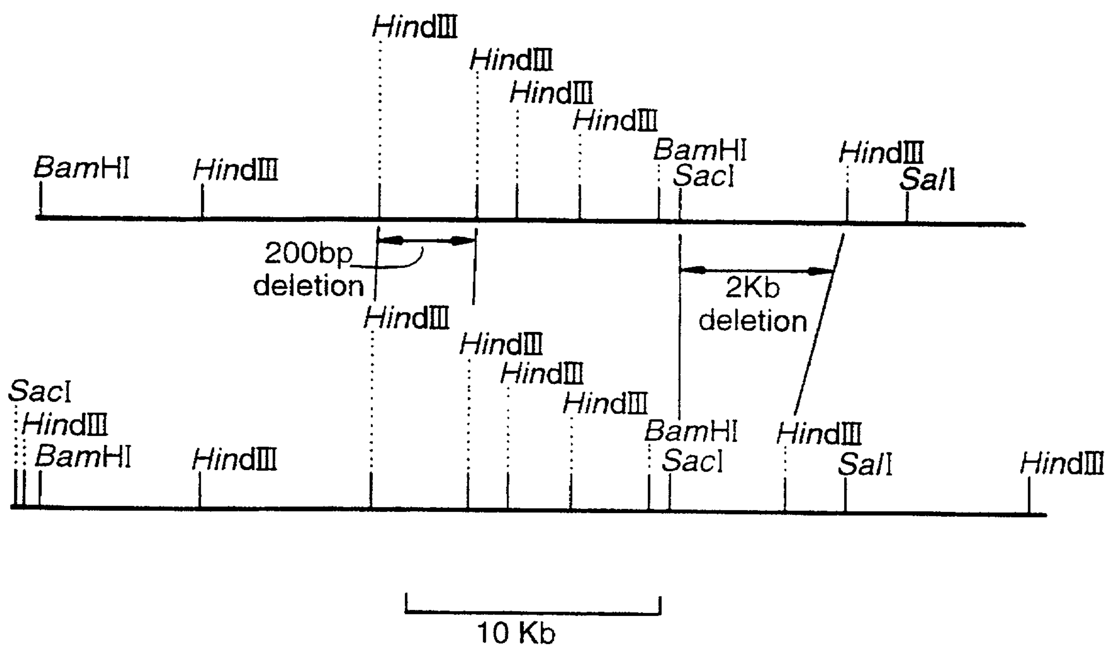
34261	GTTTCTTCTG	TGAGTGCATC	ATATTGCAAT	ACCTCGGTTT	TTTCTCCCGG	CGGTACATCA
34321	GGCGTATTGG	GGTTACCGTG	ATCGGCAATT	TCTTCCGGTG	TCGCCTCACG	GACATATTGC
34381	CAGGCATTCT	CATAAACCGG	TAAATCAGGT	GAAATATTGC	GGTCGGGAAT	ATGCCAGCGT
34441	TCAACCCAGC	CGATGTTTTT	AAAAACCGCG	CTATCATAAA	TGACATACCA	GGTTTGACCA
34501	CCAGATTGAT	TCTGCCAGGC	AACCAGAGAT	GCGCCTACTT	CGCTGCTGGC	GTCAGACATC
34561	GCTTTAATTG	AAGGGTATCG	ATAAACATTT	TGAGACATAA	TTTCACTTCC	GGCCCCGTTA
34621	TATTCCGGGG	CCGGCTCCTG	ATATCAGTTA	GAATTGTCTT	GTTTTAATTG	ATGTTTATTC
34681	AGACGGCTAC	GAACCTGCTG	GCTGAACTCA	TTACTTCCGC	CACTCACATC	ACGCGCGGTA
34741	TAACGCAGAT	GGAGGATAAT	ATCGCTCAGC	GACTCCAGCA	GCTGATCCTG	ATCGGAACCG
34801	AATTCCAACT	TCCACTGTGA	AATGGCGCCT	GTCCCTTCAA	AAGGCAGGAA	AAGTTCATCA
34861	TCAAAATTGA	GCCTGAACAT	GCCGCTGTCT	TCCATGGCCG	TTGAAATCAC	CACACCTTGA
34921	TTAGCCTGTA	CGTTCAGCAA	AACGTTTTCG	GGTTTGGTGT	ATTCCAAGGG	GTTAAGCAAA
34981	TAATCGATAG	TTTTTAAGTC	AGCAGTACTG	TAAAGCGTAT	TGCTGAGTTG	TACCAGTGAA
35041	GCCCGTACAT	CTTCATAAGG	CCCCAGCAAT	GCGGGCAATG	ACAGCGCTAC	GGTTTTTATA
35101	CGCCGATCAG	CGTGGGTCGG	ATAATCGCGC	AAGAACATTT	CGGCGCTCAG	TAAGAAAGTG
35161	AATGAACCCG	TACTCTTGCC	AATTTCCCAC	TGTGATGATG	TCAGTAATGA	TTTTACCGAT
35221	ATGGTTTTTA	TGATCTCCAG	ACGTCTGGTG	TTATGTTGCA	AATACGCCTG	ATCCATCCGT
35281	TGTAAGGCTA	ATTTCAGATG	TTCTCCGACC	AGCAGCCCCT	GATAAAGATC	ATTCCAGAGA
35341	CCACTTTGGA	CGAAATTCAT	ATCATACTGA	CCTGTTTCGT	ACTGCCAGGA	GGCTTCGGCC
35401	AGTAAACAGA	GGGAATTAAC	CGCATCATAG	GCTTGCAGGT	AAAGCCGGAG	ATTTGGCTGA
35461	TCATCCACAT	GTATAACGCA	TCATTGGTAN	ANTTGTTCNN	NNNNNNNNNN	NNNNNNNNNC
35521	CCGAAGCATA	CCGCCAAGAC	CATCCCCCCG	ACGGCCAGAC	CGAAAATATT	GGGAACCATA
35581	TCCGCCACAG	CGGCCGCAGT	GGCGGCTGAC	TGGGCAGCGA	TCACACCTTC	AGCCGCTCTT
35641	GATTGTAATG	CGATAACTTC	CTGCTCGGTG	ATGGAGATGT	TTTCATCATA	GAGCGATTTA
35701	TAGTGTTGCT	GGCGCTCCTG	AGCGGCCCGT	CGGCTGATGG	TCAGTGCATC	CAATGAAGCC
35761	TGTTGCATGT	CAATCGCTTG	CTGTTGCAGA	TTGCGGGTAA	AGCTGTACAG	CCCCAGTTGC
35821	TGCTGCATAC	GGAAGTGTTC	AAAATCGGTA	TTGTCTTTTT	TCTCCAGCAA	ACTCAGTAAC
35881	GTGCTGCCGT	ACTGAATCAG	CGTTTCTGCG	GCCTCTTTTG	CCCGGCTCAT	GATCGGGGTG
35941	AAACGATAAT	TCGGGATTGC	CCGGCGTTTC	ATGCCCGCCA	TACGATTAGC	CACAACACGC
36001	TGGTAACGCT	GCCTGAGCAG	ATCTTGCGGG	CTGATGGGTT	CATCGTATAA	TCCGGCCGGA
36061	AACTCTTTAC	CATCCAAGGT	CAGGTTATGA	CGTAAGTTAT	ATAGACGCTG	ATCCAACATT
36121	TGCCACAGTT	TGAGATATTC	CGTATCAACA	GGTTTGACAA	ATAAATCAGA	CGGTGCGGCA
36181	GAGACGGATG	TATCATATGT	CACAGGCAGA	AGTGGCACGT	TGCTGACAGT	AAGCATTAAC
36241	TCCTGTGCCC	GTGCTTCACT	GTTTTCATAC	AGAGCCACAT	CTTGCAGCGT	ACGGGGTTGC
36301	CAGTTTGCCG	CGAGCAGAAT	ATCAGGGCTG	GTACCCAGTA	ACATATTGAC	GGAGTCATAG
36361	ATCTGCTTGG	CGACAGTACG	TGCACTGGAT	GTCAGCTTAC	GGTATTCCAT	GTCTCCCTGA
36421	TCTAACAGAT	TCTTGACATA	GAAACGGAAT	ATTGCTTTCC	GGTAGTGAAT	GGGTTCACTG
36481	GCTGCAATGG	CATCCGGATC	GGTTGGTTCA	ATTAACATCC	GGTACACGGT	GGGTGGAGGA
36541	TCAATAATTG	GCCGTGAATT	CCAGTAACGC	GGTTTACCTT	GGTTGCTGGC	CTGAACAAGT
36601	TCATCTTCCA	GCGGATTAAA	AATATAGTGC	AGCCATTCGG	TGGCCTCTTT	TAATCGTTGT
36661	TCTATATTCA	GTCGCCACGC	GACCAGAAAT	GGCATATGGA	AAAACAGTTC	CCAGAAATAG
36721	ATCCCATTTG	CGCCATTTAA	ATCAATCGGC	GTAGGGAATG	AACCGGGTAT	AGGCTGTTCG
36781	GTAATAAGCT	GTGTATTCCA	GCTCAGTACC	TGCGGGATAC	CCTGACTGGC	AATGGCGATC
36841	AGTTTTTTTG	CAAACAGTGT	ATTAAGGCGA	ATGTTTTGTG	GCGCGTTATC	AGTTTCATCT
36901	GCGGGGAAGG	AAAGGAATTG	CACCTGATCC	TGTTCATTGA	GTTTAATCAG	TTCGCGAATA
36961	TGCATACCGA	TTCTGAACTC	TTGAGTACAG	CTGGCACTTT	CATTGCCAAC	ACCACCTTTG
37021	GGCTTAAAGA	GAAGTTCGGC	TTTCAGGGTG	ATTCGATTAT	CCGACCCCAG	CTTGATTGAT
37081	GGATAGGTTA	AATCAAGAAC	TTTTTCGCTC	AGTACCAGTG	GTTGTTCATC	CAAGACAGTA
37141	TTATCGTGCA	TCAGCCGGAA	AGAACCGTTG	TAATATTGAT	GATCTTCTAT	CGCACCAAAC
37201	TTAAAGTCAG	ATTGAGCGAC	AATCTCCAGT	GTGTCATCAG	TGCCATGAAC	AAAATTGACA
37261	ATCAGTTTGA	TACTGTCTTT	GCCGAAATCA	GGGTTCATTC	CGGTTTGGAT	TCTCCGGCAA
37321	TAGGAAAGCG	TTCTTCCCGG	GTTGCCGGAT	AGAGCACCAT	AGTACGGTAA	TCGATAGGAT
37381	TGCCTTAAGG	CATCCTTGTG	TTCACGTGAG	TAATACCAGA	CCAGGTTGCC	GACATATTTT
37441	CCTTTTCGTC	CATCAGCATA	TTGGTCATCC	GGCAAATCAG	TAATTTCTAC	CAGCAGTGTA
37501	TCGCAGACAT	AACCGAAGGC	TTCGTCATAA	TCATAATCCT	TACCTTTCTT	ATCTGTCCCC
37561	TGAAGACGGA	CAAACGGAAC	CAGAGCCAGA	AACGGGTTAT	GCGGGTCTTG	CTGTATATCC
37621	ATCACAGCAA	CCATCTGGGC	CATCCGGTAT	TGCAGATGTC	TTCGCGCAGA	ATGGTGGGTG
37681	TACTCCAGCT	GCCATCATAT	TTGGCATAAG	CGATTTTGAT	CCGGTCAGGA	ACGGTGTGGG
37741	AGGAACCCAA	TCACCCGCAC	TAGGCTCAAC	GTTTTGGTTA	TGCAGTGATA	ACGCAGTTGT
37801	ATCTTTAGTT	TCAGACTGTT	CTTCAACTTC	CGTCCAGGCA	ATATACAGGC	GATTATTCAG
37861	GAAAATGGGG	CGTATCAAAT	TGGGGTCTAC	GCTGCCCAAT	GGCAGGTCAA	TAGGTTTCCA
37921	CTCGCTCCAG	GCATTGGGAG	ATAACGCATC	GGTATCAGGA	TGGCGTATCG	AAAGATTCAG
37981	TGAACGCCAG	TAATATTGGT	ATGGCTGTGT	ACGGGTACGT	CCGACAAAGA	AGAACTTATC
38041	GCGTTTGATG	TTAACACCAT	CTTCATAACC	TGCGATAACT	TTCAGGTTAC	TGACATCTTC

Fig.2.

```
38101  AAAATTATTC AGATAACCGA GCACCGCTTG TTGTACAGAA TCTTCGGTAA TTTTTCCCTG
38161  ATTAAGGGCA CTTTCCAGTT GGAAGAAGAA TTCTGTTTTA TTCAGGCGTA ACAGGGGTTC
38221  CAGATAGCTT TCCGGATAAG TCCGTAATAA GCGATCCC
```

N=unspecified base

Fig.3.



UTILITY
Original U.S. or PCT D/O
Foreign Priority

DECLARATION, POWER OF ATTORNEY AND POWER TO INSPECT

As a below named inventor, I hereby declare:

that my residence, post office address and citizenship are as stated below next to my name;

that I verily believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the invention entitled: **PESTICIDAL AGENTS**

the specification of which [check one(s) applicable]
X was filed 27 August 1997 as International Application No. PCT/GB97/02284 [on which U.S. Appliction No. 09/242,843 is based]
X and was amended by Amendment filed 02 October 1998 [under Article 34] (if applicable); [or];
_____ is attached to this Declaration, Power of Attorney and Power to Inspect;

that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above; and

that I acknowledge my duty to disclose information which is material to the examination of this application in accordance with Rule 56(a) [37CFR§1.56(a)].

CLAIM UNDER 35 USC §119: I hereby claim foreign priority benefits under 35 USC §119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)

Application No.	Country	Filing Date Day-Mo-Year	Yes - No
9618083.1	GB	29 August 1996	X

POWER OF ATTORNEY: As inventor, I hereby appoint **DANN, DORFMAN, HERRELL AND SKILLMAN, P.C.** of Philadelphia, PA, and the following individual(s) as my attorneys or agents with full power of substitution to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: **Patrick J. Hagan, Reg. No. 27,643 and Henry H. Skillman, Reg. No. 17,352.**

POWER TO INSPECT: I hereby give **DANN, DORFMAN, HERRELL AND SKILLMAN, P.C.** of Philadelphia, PA or its duly accredited representatives power to inspect and obtain copies of the papers on file relating to this application.

SEND CORRESPONDENCE TO: CUSTOMER NUMBER 000110.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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